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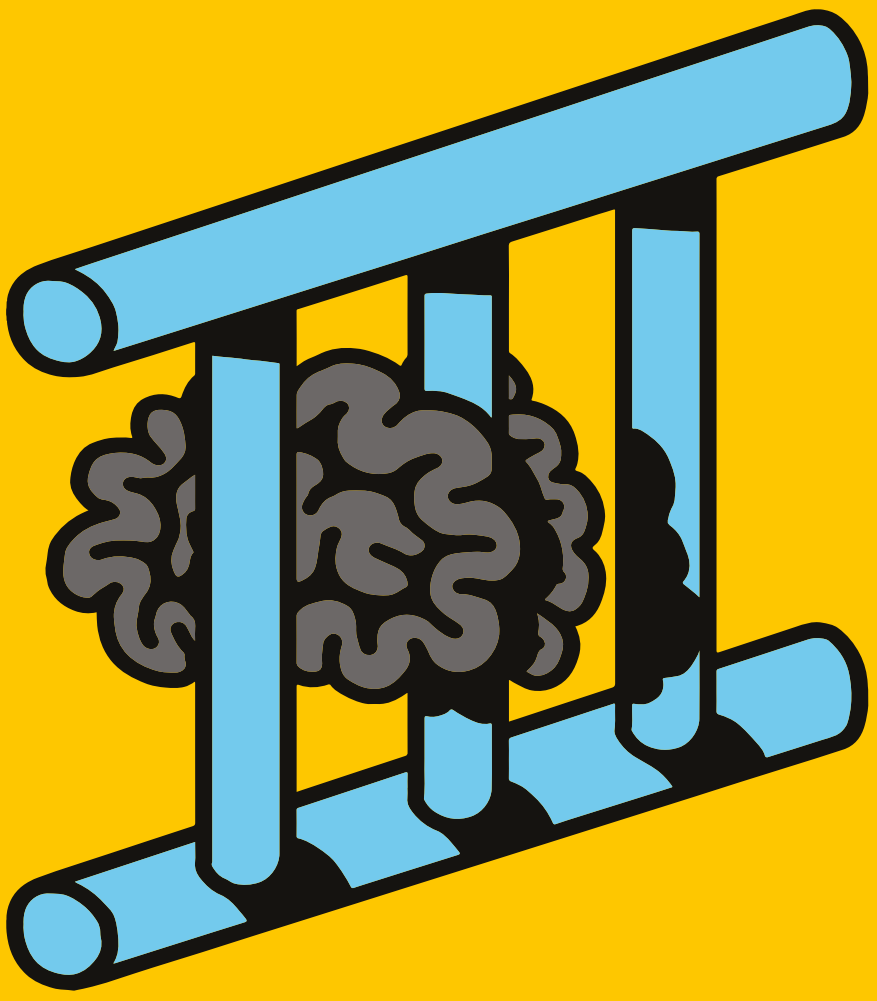
Multi-problem young adults

Neural correlates of antisocial behavior



Josjan Zijlmans

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VRIJE UNIVERSITEIT

Neural correlates of antisocial behavior in multi-problem young adults

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aan de Vrije Universiteit Amsterdam,
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door

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geboren te Rotterdam

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Contents

Chapter 1: General introduction

Multi-problem young adults and neurobiological research into antisocial behavior

Young adulthood is a challenging period in life when mental disorders (Tanner et al., 2007), psychiatric comorbidity (Newman et al., 1996), and offense rates (Loeber, Farrington, & Petechuk, 2013) peak. Most emerging adults are sufficiently resilient to reach adulthood healthy and capable in spite of the difficulties they encounter (Arnett, 2007). For multi-problem young adults this is not the case. This group is defined as individuals aged 18 to 27 without a stable income nor structural daily activities and significant issues in at least one of the following life domains: addiction, mental health, social network, and justice (Luijks et al., 2017). They are unable to handle the demanding requirements of the transition from adolescence to adulthood successfully and suffer from a plethora of problems. They often have a history of childhood adversity, service use, and school troubles, and suffer from a variety of problems including psychiatric disorders, unemployment, homelessness, low education, a poor social network, substance abuse, and delinquency (van Duin et al., 2017). One of the most pertinent problems in multi-problem young adults, as defined in this thesis, is the occurrence and persistence of antisocial behavior. Antisocial behavior is a heterogeneous concept that includes psychopathic traits, aggression, and criminal behavior. Psychopathic traits can be measured across three factors: affective callous-unemotional traits, impulsive-irresponsible traits, and grandiose-manipulative traits (Cooke & Michie, 2001) and relate to differential neurobiological processes (Blair, 2013). Aggression can be subdivided into proactive aggression (unprovoked, goal-directed) and reactive aggression (retaliatory; Dodge, 1991), which constitute separate (though overlapping) forms of aggression with different correlates and outcomes (Merk, Orobio de Castro, Koops, & Matthys, 2005). Antisocial behavior has major consequences for individuals themselves as well as victims, and is extremely costly to society (Kiehl & Hoffman, 2011; McCollister, French, & Fang, 2011). Current interventions targeting populations with antisocial behaviors are of limited effectivity and it is largely unclear what moderators are relevant to treatment (Lipsey, 2007). Neurobiological research may help better understand antisocial behaviors (Popma & Raine, 2006) and neurobiological variables can potentially function as treatment moderator (Cornet, De Kogel, Nijman, Raine, & Van Der Laan, 2014).

Even though emerging adulthood is viewed as a distinct developmental phase (Arnett, 2000), relatively little research into the neurobiology of antisocial behavior is dedicated specifically to the age range it comprises, that is 18 to 27 year olds, nor to the occurrence of multiple problems simultaneously. Studies on antisocial behavior often investigate either children and adolescents (usually diagnosed with a behavioral disorder), adults with psychopathic or delinquent problems, or convenience samples with varying amounts of aggressive behavior or psychopathic traits. This is especially

true for neurobiological research. Exceptions are scarce (though see for example (Dillon et al., 2009) and when samples do consist of young adults, usually they concern healthy subjects rather than clinical or high risk populations (e.g. (Osumi et al., 2012; Rilling et al., 2007). Of course, neurobiological research in participants within different age spans can still be informative in understanding the problems these young adults present with. For instance, childhood adversity has been shown to be related to both structural and functional brain abnormalities later in life (Hart & Rubia, 2012). Maltreated children show increased amygdaloid activity to angry and fearful faces (McCrory et al., 2013; Tottenham et al., 2011); a neural abnormality that remains into adulthood (Dannlowski et al., 2012). However, to understand how such changes occur and to what extent they are relevant throughout development, research specifically in young adults is warranted.

Another issue is that previous research has mainly investigated antisocial behavior in a dichotomous manner. For example, adolescents with conduct disorder are compared to healthy controls (e.g. Decety, Michalska, Akitsuki, & Lahey, 2009), psychopaths are compared to non-psychopaths (e.g. Birbaumer et al., 2005), or violent criminals are compared to controls (e.g. Chan, Raine, & Lee, 2010). Because sample sizes are usually small and research findings often conflicting, researchers have been focusing on extreme behaviors in order to explicitly investigate specific aspects of antisocial behavior (e.g. De Wied, Van Boxtel, Matthys, & Meeus, 2012; Passamonti et al., 2010; Sebastian et al., 2012). However, the dimensional structure of externalizing (amongst which antisocial) behavior is evident (Fergusson, Boden, & Horwood, 2010; Krueger & Markon, 2013) and specifically psychopathy is thought to be represented better dimensionally than taxonomically (Edens, Marcus, Lilienfeld, & Poythress, 2006; Guay, Ruscio, Knight, & Hare, 2007; Murrie et al., 2007). Categorical analyses on dimensional data are limited because when extreme groups are analyzed they disregard the variation of the middle (Coghill & Sonuga-Barke, 2012), when data are split statistical power decreases (Altman & Royston, 2006), and cutoffs are necessarily arbitrary. Additionally, many studies focus on a single construct (e.g. psychopathy as one rather than consisting of different factors), although it is believed that different facets of antisocial behavior interact with each other (Hyde, Shaw, & Hariri, 2013). More recently, large, well-powered, and dimensional studies involving multiple constructs (e.g. Maurer et al., 2018; Prätzlich et al., 2018) are being published to overcome these limitations and this thesis is part of that ongoing effort.

Thus, we aimed to use a dimensional approach and three neurobiological measurement techniques (i.e. functional magnetic resonance imaging, electroencephalography, and measurements of the autonomic nervous system) to disentangle the associations between antisocial behaviors and pertinent processes found to be dysfunctional in antisocial populations: morality, cognitive control, and

the basic functioning of the autonomic nervous system. Additionally, we aimed to study the predictive value of neurobiological measures for criminal recidivism. The rest of this chapter introduces these processes and provides a brief background for the neuroprediction of criminal recidivism.

Morality

Research in predominantly healthy population suggests that areas throughout the brain perform various functions in moral processing. The amygdala and ventromedial prefrontal cortex are relevant to the processing of emotional information; the dorsolateral prefrontal cortex is engaged in cognitive control and utilitarian decision making; the cingulate is involved in mediating the emotional and rational components of morality; and the superior temporal gyrus is relevant to intentionality and thinking about others (Fumagalli & Priori, 2012; Greene, Sommerville, Nystrom, Darley, & Cohen, 2001; Harenski & Hamann, 2006; Heekeren, Wartenburger, Schmidt, Schwintowski, & Villringer, 2003; Moll et al., 2002). With regards to antisocial behavior, much research has been invested in (im)moral behavior in psychopathy. The dominant view holds that the moral dysfunction of psychopathic individuals can partly be explained by aberrant neural functioning of the amygdala and ventromedial prefrontal cortex (Blair, 2007). Through a process of stimulus-reinforcement learning, the amygdala is thought to associate actions that harm others with the aversive reinforcement of the victim's distress. The information of reinforcement expectancy is then processed by the ventromedial prefrontal cortex, which results in healthy individuals avoiding to perform moral transgressions. When amygdala functioning is disrupted, the vmPFC fails to appropriately represent the valenced information, leading to immoral behavior.

Harenski and colleagues have performed a series of studies in antisocial samples of incarcerated male adults (Harenski, Harenski, Shane, & Kiehl, 2010), incarcerated adolescents (Harenski, Harenski, & Kiehl, 2014), and incarcerated women (Harenski, Edwards, Harenski, & Kiehl, 2014a). Participants were presented with pictures depicting immoral (i.e. negative, immoral acts), non-moral (i.e. negative, but not immoral acts), and neutral situations. When contrasting both the moral and nonmoral pictures with the neutral pictures, negative relations were found between psychopathy and amygdala activity in the adolescent and female samples; between psychopathy and cingulate and superior temporal activity in the female sample alone; and between psychopathy and medial frontal activity in the adult male sample. However, when specifically looking at the moral versus nonmoral contrast, only the negative relation between psychopathy and medial frontal activity in male adults remained. Thus, these studies mainly show a relation between psychopathy

and neural processing of negative valence in general, rather than morality specifically. Similarly, another study investigated brain activity during the making of moral judgments by community volunteers (Glenn, Raine, Schug, Young, & Hauser, 2009; Glenn, Raine, & Schug, 2009). The authors found that psychopathic traits were negatively related to amygdala, medial frontal, and cingulate activity, and positively related to DLPFC activity when contrasting "moral personal emotion-provoking" and "moral impersonal less emotional" dilemmas. Here, emotion is specifically part of the contrast researched, suggesting brain activity varies with psychopathy depending on what type of moral situation is considered.

In sum, a theoretical basis for amygdala and vmPFC dysfunction underlying moral dysfunction in psychopathy exists (Blair, 2007), but neuroimaging results vary with samples. Moreover, reported contrasts in different studies are hard to compare directly and, in some cases, may not solely represent moral processing.

Cognitive control

Conjointly with moral problems, antisocial populations tend to have trouble with several cognitive control processes, or executive functions (such as inhibitory control and behavior monitoring; e.g. (Blair, 2005; Wilkowski & Robinson, 2007) which are required to monitor performance and pursue goal-directed behavior. An essential part of performance monitoring is error processing, which refers to the ability to adequately process negative consequences in order to appropriately adapt subsequent behavior (i.e. learn from your mistakes). Two main electroencephalographic components are involved in error processing. The first is the error related negativity (ERN), which occurs approximately 25-100 milliseconds after an incorrect response is made, and is thought to be a marker of early, automatic error detection (Bernstein, Scheffers, & Coles, 1995). Its magnitude reflects the ability to monitor ongoing behavior (Holroyd & Coles, 2002) and is thought to be involved in the emotional or motivational significance one attributes to an error (Hajcak, Moser, Yeung, & Simons, 2005). The other is the error positivity (Pe), a positive component that occurs 200-400 milliseconds after the incorrect response is made and is associated with becoming aware one has made a mistake (Ullsperger, Harsay, Wessel, & Ridderinkhof, 2010). A reduced ERN in antisocial populations may indicate that errors are perceived as less meaningful or motivationally-relevant by these individuals, which may underlie the persistence of disruptive behavior despite the adverse consequences. Similarly, a reduced Pe may be indicative of diminished conscious awareness of errors, limiting the potential to learn from them.

Results regarding the ERN and Pe in psychopathy have been somewhat diverse. Some authors have found impulsive psychopathic traits to be associated

with a reduced ERN (Bresin, Sima Finy, Sprague, & Verona, 2014; Pasion, Cruz, & Barbosa, 2016) in convenience samples, whereas others have found an association between interpersonal psychopathic traits and an increased ERN (Pasion et al., 2016). Within antisocial samples findings have mainly been non-significant (e.g. Maurer 2018, Brazil 2011), but there are notable exceptions (Munro et al., 2007; Von Borries, Brazil, Bulten, Buitelaar, Verkes, & de Bruijn, 2010). With regards to the Pe, studies in violent adult male offenders (Brazil et al., 2009), incarcerated adolescents (Maurer et al., 2015), and incarcerated female offenders (Maurer et al., 2016) have found a negative relation between psychopathic traits and the Pe, indicating that psychopathy is associated with diminished error processing. But again, there are exceptions (Heritage & Benning, 2013; Munro et al., 2007) and one study even found a positive relation (Steele, Maurer, Bernat, Calhoun, & Kiehl, 2015).

In short, although there is a body of literature supporting the notion that neural error processing deficits are present in psychopathy, it is not yet clear how these deficits relate to the different psychopathic factors in different populations. Dimensional studies incorporating several factors simultaneously may shed light on this question.

The autonomic nervous system

Another neurobiological process that has been investigated in relation to antisocial behavior in children, adolescents, and adults is the autonomic nervous system. The most commonly used measure is heart rate (HR), but several other measures of the autonomic nervous system are distinguished. Sympathetic activity of the autonomic nervous system can be measured using skin conductance levels (SCL) and the length of the pre-ejection period (PEP; time between onset of ventricular depolarization and opening of the aortic valves). Parasympathetic activity of the autonomic nervous system can be measured using respiratory sinus arrhythmia (RSA; the variability in heart rate between expiration and inspiration). Two large meta-analyses including over a hundred studies have been published on antisocial behavior and the autonomic nervous system. In one of them, lower HR in rest and lower HR during a stressor were found to be related to antisocial behavior in children and adolescents (Ortiz & Raine, 2004). The other meta-analysis looked at both heart rate and skin conductance and differentiated between aggression, psychopathic traits, and conduct problems (Lorber, 2004). Lower HR was found to be related to aggression and conduct problems, but not to psychopathy. On the other hand, lower resting SCL was found to be related to psychopathy, but not to aggression or conduct problems. A more recent meta-analysis also found a relationship between low resting heart rate and antisocial behavior (Portnoy & Farrington, 2015). The theory that best fits these general results

is the fearlessness theory (Raine, 1993), which states that antisocial behavior is partly due to autonomic hypo-arousal. The lower resting HR and specifically lower HR reactivity to stress in antisocial individuals is indicative of a lack of arousal when it is needed. In other words, antisocial people tend not to get aroused enough in order to appropriately deal with a situation. For instance, if punishment does not cause sufficient arousal, one will not sufficiently learn to avoid certain situations or refrain from certain actions.

Authors have also investigated how subtypes of antisocial behavior relate differently to ANS activity. For example, (Scarpa, Haden, & Tanaka, 2010) differentiated between reactive and proactive aggression, and found that reactive aggression was related to lower respiratory sinus arrhythmia and lower skin conductance, whereas proactive aggression was related to higher respiratory sinus arrhythmia. Another differentiation that is being made is between groups high and low in callous unemotional (CU) traits. Antisocial youths high in callous unemotional traits present with more severe antisocial behavior and this behavior is more likely to persist than in those with low CU traits (Frick, Cornell, Barry, Bodin, & Dane, 2003; Frick & White, 2008). (De Wied et al., 2012) investigated the autonomic activity in children with a behavior disorder and either high or low on CU traits. They found that adolescents with high CU traits had higher RSA. Additionally, they looked at the autonomic responsiveness in reaction to viewing emotional clips (happiness, sadness, anger) and found that adolescents with high CU traits showed less HR responsivity as a response to a sad video clip.

Overall, both basic functioning and reactivity of the ANS seem to be of relevance to antisocial behavior, but it is less clear how effects differ across types of antisocial behavior as only few studies differentiate between different psychopathic factors and aggression types (Portnoy & Farrington, 2015). In addition, the psychopathic factors as well as variants of aggressive behavior are known to be correlated amongst each other, but often not used in the same studies. It remains unclear whether these different antisocial behaviors have overlapping or independent associations to aberrant autonomic functioning.

Neuroprediction

Not only have neurobiological measures been cross-sectionally related to antisocial behaviors, longitudinal studies have also been performed with results indicating that some measures may be viable as predictors of long-term antisocial behavior. Unsurprisingly, the best studied process is the basic functioning of the autonomic nervous system. Over forty years ago, the first evidence was already provided that lower heart rate in childhood is predictive of delinquent behavior later in life

(Wadsworth, 1976). Since then more evidence for this association has accumulated. Autonomic hyperarousal in adolescence (age 15) has been shown to be a protective factor against criminal behavior later in life (age 29; Raine, Venables, & Williams, 1995), whereas autonomic hypo-arousal at age 3 has been shown to be a risk factor for aggression at age 11 (Raine, Venables, & Mednick, 1997). A seminal study in more than 700.000 men showed that low heart rate at age 18 predicts violent delinquency later in life (Latvala, Kuja-Halkola, Almqvist, Larsson, & Lichtenstein, 2015).

Recently, researchers have started investigating the predictive value of neurobiological indices of cognitive control for delinquency. Lack of cognitive control, or behavioral disinhibition, is a risk factor for delinquency and measuring cognitive control processes on a neural level rather than a behavioral level may capture a different part of the process and improve prediction. One study found that decreased activity in the anterior cingulate cortex (ACC), as measured with fMRI during an inhibitory (Go-Nogo) task, was predictive of rearrest in criminal offenders (Aharoni, 2014; Aharoni et al., 2013). In a subsample of the same cohort, the ERN and Pe in response to errors as measured with EEG were also included in the analysis. Here, researchers found the ERN not to be predictive of rearrest, but they did find a larger Pe to be predictive of rearrest (Steele, Claus, et al., 2015).

Studies that include both a broad selection of known risk factors for criminal recidivism, as well as a series of neurobiological measures to investigate whether neurobiological parameters predict delinquency over and above psychosocial factors are lacking in the literature.

Taken together, few studies focus on antisocial behavior in multi-problem young adults, whereas this is a worrisome group in a specific developmental phase. Neurobiological research in groups of participants that present with similar problems is available, but suffers from several limitations. Most notably, the majority of studies approached these problems using dichotomous categorizations (e.g. children with behavioral disorders versus healthy children, or criminal psychopaths versus criminal non-psychopaths) rather than continuously and sample sizes have often been small. We intend to overcome some of these limitations and help disentangle the associations between several antisocial traits and the neurobiological correlates of three pertinent processes in the problematic behavior of multi-problem young adults, namely morality, error processing, and the basic functioning of the autonomic nervous system. Additionally, we aim to use these neurobiological data to test predictive models of criminal recidivism, contributing to the knowledge base needed for risk assessment. To do so, we gathered data in a sample of 127 multi-problem young adults (age 18-27), who are part of a larger cohort of 696 participants (Luijks et al., 2017). Participants were recruited at the start of a day treatment program at De Nieuwe Kans (DNK; translated as “New Opportunities”) in Rotterdam, The Netherlands. DNK provides

a multimodal day treatment program for multi-problem young adults that employs cognitive behavioral techniques and rehabilitation components such as cognitive skills training, drug treatment, and education. Participants were invited for interviews and questionnaires, and underwent both a magnetic resonance imaging (MRI) protocol at the Erasmus Medical Center and a simultaneous electroencephalographical and autonomic assessment protocol at the Erasmus University in Rotterdam. A small, healthy control group (N=27) was included primarily to assess task validity and to explore differences between multi-problem young adults and controls.

Research question

What are the neurobiological correlates of antisocial behaviors (i.e. proactive and reactive aggression, and affective, behavioral, and interpersonal psychopathic traits) in multi-problem young adults and do these neurobiological measures predict criminal recidivism?

Outline of the current thesis

This thesis comprises five studies (chapters 2 through 6) on the co-occurrence of behavioral traits in multi-problem young adults (chapter 2), the neurobiological underpinnings of their antisocial behaviors (chapters 3 through 5), and the usefulness of neurobiological measures in the prediction of criminal recidivism in this population (chapter 6).

Chapter 2 examines in a large cohort of multi-problem young adults (N = 696) how problems cluster. More homogeneous subgroups are examined in terms of childhood risk factors, baseline functioning, and outcome measures of delinquency.

Chapter 3 is the first of three cross-sectional empirical studies performed in a subsample (N = 127) of the total cohort. It investigates whether multi-problem young adults differ from a healthy control group in terms of behavioral and brain responses to moral and non-moral stimuli. Within the multi-problem group, the relationship between psychopathic traits and the neural activity associated with moral evaluation was studied.

Chapter 4 concerns the neurobiological correlates of error processing. Again, we compared a sample of multi-problem young adults to healthy controls and investigated whether psychopathic traits within the multi-problem group were related to behavioral and brain measures of error processing.

Chapter 5 is the final cross-sectional study and covers the relationship between antisocial behavior (psychopathy and aggression) and baseline functioning of the autonomic nervous system, as well as the reactivity to emotion of the autonomic

nervous system. As in chapters 4 and 5, the sample of multi-problem young adults is compared to a healthy control groups and dimensional analyses are performed within the multi-problem sample.

Chapter 6 is a formal prediction study that assesses the incremental value of neurobiological measures to the prediction of general and serious criminal recidivism. It investigates how well classic risk factors, including demographics and intelligence; previous delinquency and drug use; and behavioral traits including aggression and psychopathy, predict recidivism, and whether neurobiological measures including heart rate, heart rate variability, functional brain activity during an inhibition task, and two electroencephalographic measures of error processing substantially increase the predictive power of the models.

Chapter 2: Disentangling multi-problem behavior in male young adults: a cluster analysis

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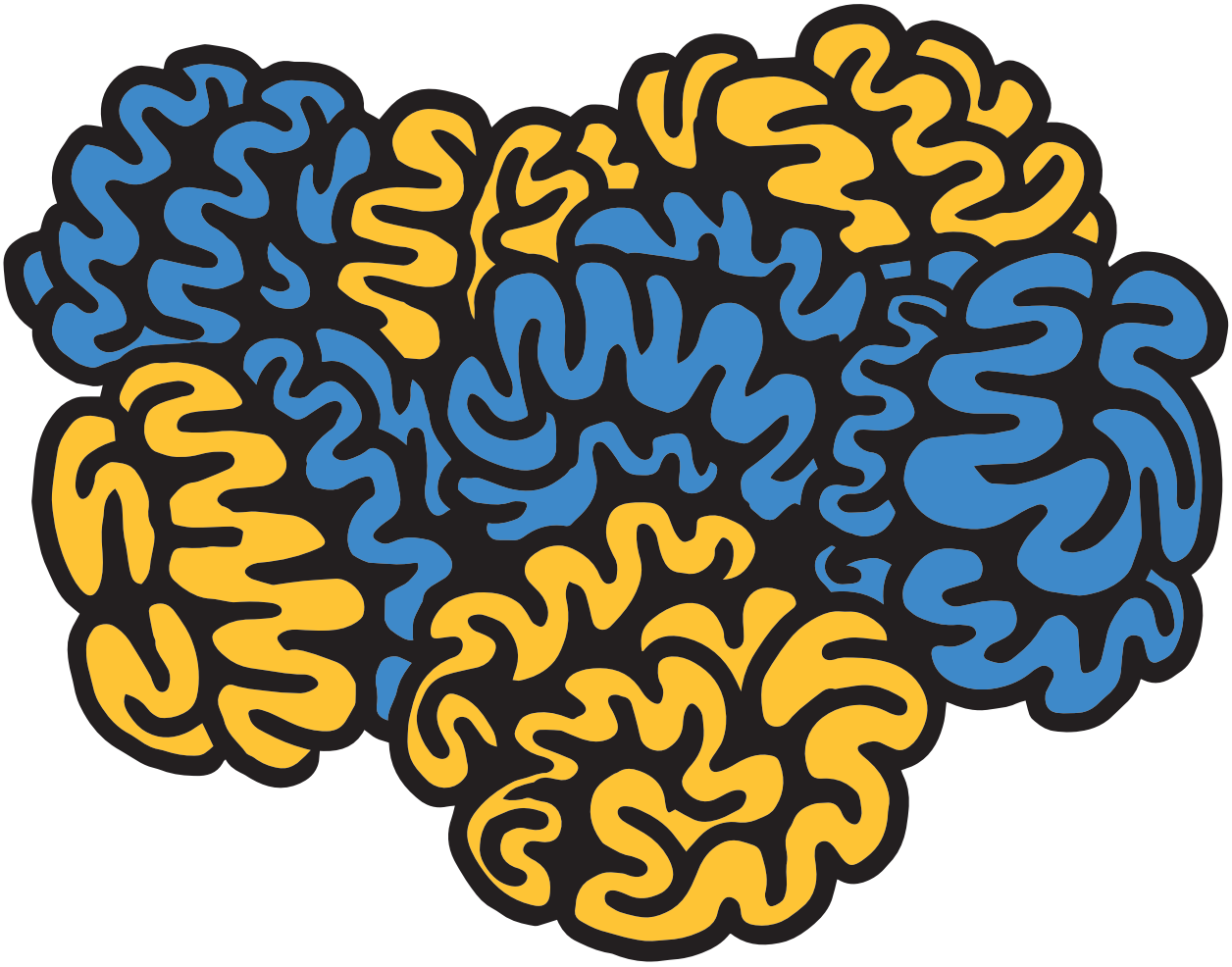


Abstract

Multi-problem young adults present with major problems across key life domains, but empirical studies investigating the nature of multi-problem behavior in accordance to ecobiodevelopmental theory are scarce. To address this gap, we performed a model-based cluster analysis on indicators spanning the key life domains Addiction, Mental health, Social network, and Justice. In a large sample (N=680) of multi-problem young adults, we identified five subgroups labelled “Severe with alcohol and cannabis problems” (4.3%), “Severe with cannabis problems” (25.6%), “Severe without alcohol or drug problems” (33.2%), “Moderate with mental health problems” (22.9%), and “Moderate without mental health problems” (14.0%). There were large differences between the severe and moderate groups in terms of childhood risk factors such as emotional and physical abuse, concerning baseline functioning such as comorbid disorders and aggressive behavior, and in the outcome measure of violent offending. Our findings indicate that multi-problem young adult behavior clusters within profiles that differ according to the severity and nature of problems. Investing in screening for clustered problems may be beneficial for early problem differentiation and selection of appropriate intervention before and during treatment programs.

Introduction

The trend that young adults are more gradually making their way into adulthood can be observed in the general population of most high-income countries (Arnett, Žukauskiene, & Sugimura, 2014): youngsters focus on identity exploration, self-development and preparation of their adult life by taking time to finish their education, becoming financially independent, and deciding about parenthood. In 2000, Jeffrey Arnett proposed the term emerging adulthood for this distinct period of the life course, ranging roughly from the late teens through the mid- to late twenties (Arnett, 2000). Emerging adulthood is now widely regarded as a critical transitional period, in which transition refers to the neurobiological process of maturation and the heterogeneous psychological and societal changes that are associated with this process (Davis & Stoep, 1997). These changes can be challenging for youngsters and there is a growing recognition that young adults should be treated as a distinct subpopulation in policy, planning, programming, and research (Stroud, Walker, Davis, & Irwin, 2015). Longitudinal research has shown that mental disorders (Tanner et al., 2007), comorbidity (Newman et al., 1996), and offense rates (Loeber et al., 2013) increase from childhood through adolescence and peak in young adulthood. However, whereas problem behavior in emerging adulthood may peak, there is also evidence that this is usually temporary and most emerging adults are sufficiently resilient to reach adulthood healthy. One study on the long-term effects of early mental health and judicial problems showed that even a large percentage of high-risk young adults were in stable marriages and jobs, and were responsible citizens in their community by the time they reached the end of their fourth decade of life (Werner, 2004).

In contrast to this predominantly positive trend for most emerging adults, there are vulnerable youngsters who are not able to handle the demanding requirements of this transitional period successfully (Osgood, Foster, & Courtney, 2010a). These young adults have extensive histories of childhood problems and have often been involved in juvenile care services that provided long-term support to them and their families. During emerging adulthood, many of them still struggle with social problems, limited capacities and/or mental health problems. Often, they lack the financial support of their also disadvantaged families which may prove essential to continue their school/college careers. Educational failure and school drop-out are important risk factors for engaging in antisocial behavior in adolescence and young adulthood (Henry, Knight, & Thornberry, 2012) and consequently for judicial interference. Therefore, it comes as no surprise that these vulnerable young adults have educational and judicial problems on top of their psychosocial constraints; they experience interrelated problem behavior across several life domains. This co-occurrence and subsequent accumulation of problem behavior can be explained in terms of theories following an ecobiodevelopmental paradigm (Jessor, 1992; Monroe & Simons, 1991; Shonkoff

et al., 2012). Since the endorsement of a 'complexity view' of human development and (mental) illness by Engel (1977) and the introduction of the bioecological model by Bronfenbrenner (1979), these theories not only address biological but also social, psychological and behavioral dimensions of problem behavior. In 1988, the first empirical evidence for a 'multi-problem' construct was found (Donovan & Jessor, 1985); delinquency, substance abuse and sexual risk behavior were shown to form a problem syndrome in both adolescence and young adulthood. Later research linked mental health problems to juvenile criminal behavior (Doreleijers, Moser, Thijs, Van Engeland, & Beyaert, 2000), and to substance abuse disorders as well (Hawkins, 2009). Studies in the last two decades have consequently investigated delinquency, mental health problems and substance abuse in young people as separate (Lee, Festinger, Jaccard, & Munson, 2017; Mulder, Vermunt, Brand, Bullens, & Marle, 2012; Odgers et al., 2007; Zijlmans et al., 2017) as well as interconnected problem domains (Dembo, Wareham, Schmeidler, & Winters, 2016; Hawkins, 2009; Mun, Windle, & Schainker, 2008; Potter & Jenson, 2003; Vaughn, Freedenthal, Jenson, & Howard, 2007). In addition, since young adult social development is marked by an extensive expansion and modification of social relationships (Lane, Leibert, & Goka-Dubose, 2017), social network problems have recently been linked to the above-mentioned key life-domains as well (McPherson et al., 2014). Also, multi-problem behavior has been shown to be highly related to multiple interrelated childhood and context factors such as Adverse Childhood Experiences (ACEs) such as family dysfunction (Kalmakis & Chandler, 2015) and child maltreatment (Gilbert et al., 2009), high residential mobility (Perkins, 2017), academic failure (Baggio et al., 2015), poverty (Font & Maguire-Jack, 2016), service use (Garland, Aarons, Brown, Wood, & Hough, 2003), and unemployment (Liu et al., 2013).

To deepen our insight into the intricacies of multi-problem behavior, statistical methods such as cluster analysis can be used; such methods aim to identify subgroups of individuals with different (risk) profiles. Recent literature on this topic can roughly be divided in studies conducted within community-based normative samples versus studies within high-risk samples. One of the few studies that attempted to investigate population heterogeneity was conducted by Mun and colleagues (2008). They showed that within an adolescent community sample a small multi-problem group who experienced an accumulation of delinquent behavior, sexual risk behavior, substance use, and mental health problems could be identified (Mun et al., 2008). There was a remarkable continuity of risk and dysfunction within this group from adolescence to young adulthood. The finding that a distinction in profiles of youth development is useful was replicated by Berzin (2010) in a community sample of emerging young adults (Berzin, 2010). Studies within high-risk groups, such as juvenile offenders, truants, and foster youth, also distinguished several profiles differing in the extent of problem behavior and in interrelationships of co-occurring adversities such as

family dysfunction, poor peer relations, adverse psychological functioning and a low educational level (Dembo et al., 2016; Mulder et al., 2012; Potter & Jenson, 2003; Rebbe, Nurius, Ahrens, & Courtney, 2017). Specifically, within a population of emerging adults with a history of childhood contact with Child Protection Services (CPS), a group with multiple mental health disorders who were troubled by a low rate of (mental) health service use was identified by Lee et al. (2017). Van Duin & Bevaart et al. (2017) retrospectively distinguished several classes of multi-problem young adults with CPS contact during their childhood differing in their CPS characteristics, the amount of family problems during childhood and their long-term mental health outcomes (van Duin et al., 2017). In sum, these studies highlight the possibilities to inform both theory and clinical practice by constructing useful typologies for young people who experience a plethora of problems and by linking these profiles to heterogeneous childhood risk factors and adult outcomes.

Juvenile and criminal justice have already been cautiously experimenting with classifications concerning the characteristics of juvenile delinquents to inform official decisions with regard to placement setting and security level (Andrews & Bonta, 1994). However, empirical studies that can help inform judicial and clinical practice about multi-problem young adults are scarce since both the introduction of the developmental phase 'emerging adulthood' and the concept of 'multi-problem' behavior within our academic domain are relatively new. Furthermore, there are only few studies (Lee et al., 2017; Mun et al., 2008; Rebbe et al., 2017) that investigated multi-problem behavior in accordance to theory by clustering several key life-domains (i.e. delinquency, substance abuse, sexual risk behavior, mental health problems and social networks problems) and consecutively relating these clusters to well documented childhood and context risk factors, such as ACEs and service use. Finally, research that uses such risk profiles to predict meaningful outcomes for daily practice, such as quality of life, education and employment, mental health problems, and (the severity of) recidivism, is even more scarce. Thus, little is known about the compositional variations of multi-problem behavior in young adulthood, the related adversity profiles, and the corresponding implications for multi-problem young adults' functioning and treatment. Since multi-problem young adults are in urgent need of professional support (Osgood et al., 2010a) to help themselves and to unburden society, and because treatment strategies may differ in effectiveness depending on the combinations of problem behavior (Collins, Murphy, & Bierman, 2004), we must aim to disentangle multi-problem behavior in this population soon.

To address this, we aim to find meaningful clusters of multi-problem young adult behavior by analyzing problem behavior across several important life domains (i.e. Addiction, Mental health, Social network, and Justice). Although in accordance with previous studies we expect to find several problem clusters, specific hypotheses concerning the qualitative nature of these clusters within our understudied target

population of multi-problem young adults are lacking. To provide a broad and comprehensive view on the nature of young adult problem behavior we explore how the clusters relate to childhood risk factors (i.e. service use, ACEs and residential mobility) and to baseline functioning (i.e. comorbidity, and antisocial- and risk seeking behavior). Finally, since enhancing quality of life, stimulating education and employment, reducing mental health problems, and (the severity of) recidivism are important aims of multimodal interventions for multi-problem young adults (Luijks et al., 2017), these were our outcome variables.

Methods

Procedure

Participants were 696 male multi-problem young adult men (age 18-27) recruited at either the start of multimodal day treatment program De Nieuwe Kans (translated as "New Opportunities") or at an intake at the social welfare agency in Rotterdam, The Netherlands (Jongerenloket). This agency itself refers young adults to treatment programs such as De Nieuwe Kans. Individuals were eligible for participation when they met the criteria for a multi-problem definition based on scores on the Self-Sufficiency Matrix (SSM; Fassaert et al., 2014). Self-sufficiency is the capacity to create an acceptable level of functioning on eleven important life domains: Income, Daytime Activities, Housing, Domestic relations, Mental health, Physical health, Addiction, General life skills, Social network, Community involvement and Justice. It is measured on a 5-point scale with 1 indicating acute problems and 5 indicating complete self-sufficiency. The inclusion criteria were: (a) a score of 1 or 2 on the domains Income and Daytime Activities, (b) a maximum score of 3 on at least one of the following domains: Addiction, Mental health, Social network, Justice and (c) a minimum score of 3 on the domain Physical health. We excluded 16 participants who finished a higher secondary education, leaving a final sample of 680 participants. In total, four assessments over fourteen months were performed during which a battery of questionnaires and tests was completed. Here, we present data from the baseline measurement, the final follow-up after fourteen months, and judicial records (see Luijks et al., 2017) for a complete description of the study protocol).

All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. The study has been approved by the Medical Ethical Committee of the VU University Medical Center (registration number 2013.422 - NL46906.029.13) and all participants provided written informed consent. Participants

received a reimbursement of 20 euros for the baseline measurement and another reimbursement of 20 euros for the final follow-up measurement.

Indicators

As indicators for the latent profiles we employed six measures that capture the range of problems within the multi-problem definition. These measures correspond with four key life-domains (i.e. Addiction, Mental health, Social network, and Justice) in accordance to ecobiodevelopmental theory (Donovan & Jessor, 1985; Doreleijers et al., 2000; Hawkins, 2009; McPherson et al., 2014). As the SSM is an ordinal measure, which limits variability, we used continuous measures of validated questionnaires to capture the full range of variation between participants. We assessed drug and alcohol use during the past 30 days (Addiction) using the Measuring Addictions for Triage and Evaluation structured interview (Schippers, Broekman, Buchholz, Koeter, & van den Brink, 2010). To assess internalizing and externalizing problems (Mental health), we used the Adult Self-Report (ASR; Achenbach & Rescorla, 2003). This questionnaire consists of 123 items on a 3-point Likert-scale and measures internalizing and externalizing problems during the past 6 months. As a measure of social network problems, we employed the friends' delinquency scale of the friends questionnaire (Meeus & Koot, 2007; Social network). Finally, we assessed delinquency with the WODC self-reported delinquency questionnaire (Van der Laan & Blom, 2006). We employed the total score as a measure of overall lifetime delinquency (Justice).

Childhood risk factors

We performed register and record research at Child Protection Services (CPS), the Psychiatric Case Register (PCR), and Probation Services (PS) to assess what proportion of participants has been in contact with these institutions. CPS monitors youth (age 0-18) when other institutions notice concerns about the upbringing, home environment, or police contact of youth. PCR registered the use of mental health care under the age of 18. At the request of the court, probation services aim to decrease recidivism after a criminal conviction. We were able to look into files of 85%, 92%, and 96% of participants respectively. We assessed eleven adverse childhood events (ACEs) in total. Emotional abuse, physical abuse, sexual abuse, emotional neglect, and physical neglect during childhood using the Childhood Trauma Questionnaire (Thombs, Bernstein, Lobbestael, & Arntz, 2009) and alcohol abuse in the family, drug abuse in the family, police contact in the family, psychological problems in the family, domestic violence, and growing up in a single parent family were assessed with Yes/No questions. Total number of ACEs was operationalized by summing the eleven ACE items. Residential mobility (number of movements) was assessed with the residential mobility calendar (Miltenburg, Lindo, Tzaninis, & Duin, 2011).

Baseline functioning

Data on baseline functioning were gathered at the same time as data on the indicators were. We assessed whether participants have a basic job qualification (i.e. finished at least junior secondary education) based on their self-reported education. We measured IQ using four subscales of the Wechsler Adult Intelligence Scale third version (WAIS-III SF; digit symbol coding, information, block design, and arithmetic; Blyler, Gold, Iannone, & Buchanan, 2000). As a measure of comorbidity, we used research diagnoses based on DSM-IV criteria as assessed during the Mini-International Neuropsychiatric Interview (M.I.N.I.; Sheehan et al., 1997). As a measure of aggression, we employed the Reactive Proactive Questionnaire (RPQ; Cima, Raine, Meesters, & Popma, 2013; Raine et al., 2006). The RPQ consists of 23 items scored on a 3-point Likert scale. We used the Barratt Impulsivity Scale (BIS-11) to assess impulsivity (Patton, Stanford, & Barratt, 1995). The questionnaire consists of 30 items scored on a 4-point Likert scale. As a measure of psychopathic traits, we employed the Youth Psychopathy Inventory – Short Version (YPI-SV; van Baardewijk et al., 2010). The YPI-SV is a self-report measure that has been validated in young adults (Colins & Andershed, 2015). It consists of 18 items scored on a 4-point Likert scale. We assessed sensation seeking with the Brief Sensation Seeking Scale (BSSS; Hoyle, Stephenson, Palmgreen, Lorch, & Donohew, 2002), which consists of 8 items scored on a 4-point Likert scale.

Outcome variables

We assessed functioning at 14-month follow-up (response rate 78%). We again assessed internalizing and externalizing problems using the ASR. We measured quality of life using the Manchester Short Assessment of Quality of Life (MANSA; Priebe, Huxley, Knight, & Evans, 1999). We assessed whether participants were following school or were employed based on self-report. Finally, we obtained data from the Research and Policy database Judicial Documentation (OBJD) by the Research and Documentation Center (WODC) of the Ministry of Service and Justice in the Netherlands to assess registered delinquent behavior (median follow-up period 31 months). We differentiated between violent crimes, sexual crimes, property crimes with violence, property crimes without violence, destruction/public order crimes, drug crimes, traffic crimes, and other crimes.

Statistical analysis

First, to account for missing data (% missing data for indicators varied between 0 and 12%) we used multivariate imputation by chained equation to obtain 20 complete datasets. This method replaces missing values with plausible values drawn from a distribution specifically modelled for that missing value. As all indicator variables are

continuous, we used predictive mean matching to obtain the imputed values (Buuren van, 2012). We then performed a model-based clustering analysis (MBCA) in R (R Core Team, 2016) using the clustMD package (McParland & Gormley, 2016) over all imputed datasets to identify latent groups. The input variables were mean-centered and then scaled by dividing the centered columns by their standard deviations before running the analysis. This is done to prevent variables with a large variance to have more influence on the clustering than other variables. We used the Bayesian Information Criterion (BIC) and the Integrated Classification Likelihood criterion (ICL) as formal measures to inspect model fit, with higher values indicating a better fit. Additionally, substantive theory and interpretability of clusters were taken into account to decide upon the number of classes. Individuals were classified to the most likely cluster based on the highest posterior probability. To assess whether the latent groups differed on past risk factors, baseline functioning, and group outcomes, we performed ANOVAs for continuous dependent variables and logistic regression for binary dependent variables. All post-hoc comparisons were Bonferroni corrected.

Results

Clusters

Both fit statistics were best for VEI models and indicated better performance of models including more clusters (see table 1). However, inspection of the five to six cluster solutions revealed that the added profile was not meaningful as profiles were either very small or similar to other clusters. Additionally, posterior probabilities for both the five (0.93) and six (0.94) cluster solutions were very high and fit indices differed only slightly. Therefore, we decided upon the five-cluster solution for further investigation. The first and smallest cluster comprises 4.3% (N=29) of the sample. It scores high on all indicators and is set apart most from the other clusters due to high alcohol use (M = 18 days per month) and high cannabis use (M = 19 days per month). We labelled it “Severe with alcohol and cannabis problems”. The second cluster comprises 25.6% (N=174) of the sample. It resembles the first cluster as it has similar albeit slightly lower scores on the mental health, delinquency, and social network indicators. It has very high cannabis use (M = 26 days per month), but no alcohol problems (M = 3 days per month). We labelled it “Severe with cannabis problems”. The third cluster comprises 33.2% (N=226) of the sample. It has comparable scores as the second group, but lacks the high cannabis use (M = 6 days per month). We labelled it “Severe without alcohol and drug problems”. The fourth cluster comprises 22.9% (N=156) of the sample. It presents with considerably less problems than the first three groups on the delinquency and social network indicators and shows little

drug use. In addition, it shows fewer externalizing problems, but similar or even more internalizing problems. We labelled it “Moderate with mental health problems”. The fifth and final cluster comprises 14.0% (N=95) of the sample. Its profile is comparable to that of the fourth cluster, but scores low on mental health issues. We labelled it “Moderate without mental health problems”. See figure 1 for an overview of the clusters.

Table 1. Model-fit statistics

# clusters	BIC	ICL
2	-10726.23	-10795.56
3	-10159.51	-10238.91
4	-9926.23	-10031.62
5	-9499.15	-9572.22
6	-9312.26	-9386.70

Differences between clusters

As the first three clusters and the last two clusters clearly differ in severity of baseline functioning, in addition to simple post-hoc contrasts between individual groups we performed a post-hoc test between the three severe clusters versus the two moderate clusters (see table 2). When looking at childhood risk factors, all groups show similar proportions of contact with youth services, with the severe clusters having had more contact with probation services. The moderate groups have experienced fewer total ACEs, specifically emotional and physical abuse, and alcohol and drug abuse in the family. Whereas there are no differences between the severe groups, the fifth group (moderate without mental health problems) has experienced significantly less ACEs than the fourth group (moderate with mental health problems). The severe groups have had more residential movements than the moderate groups.

Regarding baseline functioning, there are no differences in basic job qualification nor IQ between any of the groups, but there are sizable differences on comorbidity and the behavioral measures. The three clusters with severe problems show larger comorbidity, greater sensation seeking, more aggressive behavior, higher levels of impulsivity, and more psychopathic traits than the two moderate clusters. Again, there are no differences within the severe clusters, but the fourth group presents with more impulsive and psychopathic behavior than the fifth group.

As for group outcomes, the differences in mental health problems between groups remain intact, but all groups score lower on both internalizing and externalizing problems than at baseline. Quality of life is similar for all groups, although slightly higher for the fifth group. There are no differences in the proportion of individuals that go to school or have a job. The severe groups show higher rates of violent crimes and destruction/public order crimes.

Table 2. Indicators, childhood risk factors, baseline functioning, and outcome measures for each cluster

	1. Severe with alcohol and cannabis problems (N=29)	2. Severe with cannabis problems (N=174)	3. Severe without alcohol or drug problems (N=226)	4. Moderate with mental health problems (N=156)	5. Moderate without mental health problems (N=95)	Omnibus F / x2	Severe v.s. moderate
Indicators							
Internalizing	76.28	72.10	70.16	79.78	37.59	.	.
Externalizing	78.83	73.13	71.39	63.01	34.05	.	.
Delinquency	48.61	40.44	40.94	10.90	14.39	.	.
Friends' delinquency	4.21	2.44	3.10	0.73	0.76	.	.
Alcohol	17.76	3.01	3.00	1.12	1.18	.	.
Cannabis	18.69	25.60	6.24	1.63	2.63	.	.
Childhood risk factors							
Known at CPS	0.65	0.70	0.68	0.55	0.70	9.21	n.s.
Known at PCR	0.37	0.30	0.29	0.32	0.32	0.98	n.s.
Known at PS	0.52	0.60[4]	0.57	0.39[2]	0.51	16.35**	***
Emotional abuse	0.55[5]	0.33[5]	0.34[5]	0.33[5]	0.19[1,2,3,4]	15.10**	*
Physical abuse	0.41[5]	0.39[5]	0.42[5]	0.29[5]	0.19[1,2,3,4]	20.40***	***
Sexual abuse	0.07	0.16	0.10	0.06	0.07	8.80	n.s.
Emotional neglect	0.76	0.71	0.67	0.72	0.63	3.22	n.s.
Physical neglect	0.34	0.41	0.41	0.39	0.31	3.61	n.s.
Alcohol abuse in the family	0.24[4,5]	0.14[4,5]	0.13	0.04[1,2]	0.05[1,2]	18.89***	***
Drug abuse in the family	0.21[4,5]	0.11	0.12	0.04[1]	0.06[1]	13.20**	**

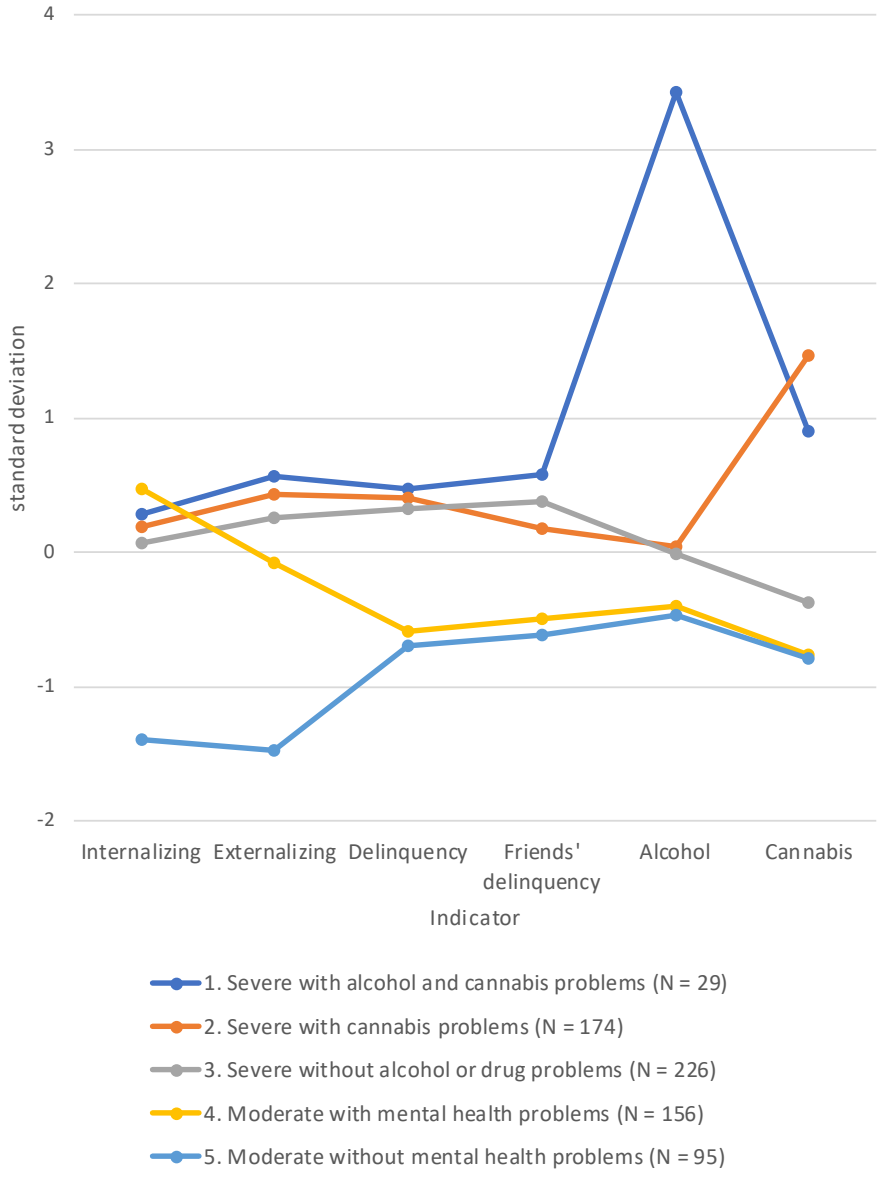
Table 2. Indicators, childhood risk factors, baseline functioning, and outcome measures for each cluster

	1. Severe with alcohol and cannabis problems (N=29)	2. Severe with cannabis problems (N=174)	3. Severe without alcohol or drug problems (N=226)	4. Moderate with mental health problems (N=156)	5. Moderate without mental health problems (N=95)	Omnibus F / x2	Severe v.s. moderate
Childhood risk factors							
Police contact in the family	0.24	0.17	0.18	0.12	0.12	5.87	n.s.
Psychological problems in the family	0.24	0.11	0.09	0.08	0.05	8.71	n.s.
Domestic violence	0.21	0.15	0.15	0.12	0.07	5.97	n.s.
Single parent	0.55	0.44	0.40	0.38	0.37	4.09	n.s.
Number of ACEs	4.41[4,5]	3.80	3.69	3.36[1]	2.98[1]	4.73***	***
Number of movements	5.45	5.21[4,5]	4.80[4,5]	3.58[2,3]	3.35[2,3]	7.38***	***
Baseline functioning							
Startqualification	0.14	0.17	0.20	0.20	0.24	2.61	n.s.
IQ	82.28	81.70	79.07	80.28	81.19	1.71	n.s.
Comorbid disorders	2.17[5]	1.93[4,5]	1.85[4,5]	1.38[2,3]	0.53[1,2,3]	12.86***	***
Sensation Seeking	19.10	19.88[5]	19.76	19.29	17.77[2]	3.45**	*
Impulsivity	68.31[5]	65.54[4,5]	65.36[4,5]	63.02[2,3]	57.97[1,2,3,4]	15.18***	***
Agression	21.66[4,5]	18.23[4,5]	18.20[4,5]	12.46[1,2,3]	9.49[1,2,3]	37.91***	***
Psychopathy	38.04[4,5]	35.23[4,5]	35.78[4,5]	31.71[1,2,3]	28.52[1,2,3,4]	22.11***	***

Table 2. (cont.) Indicators, childhood risk factors, baseline functioning, and outcome measures for each cluster

	1. Severe with alcohol and cannabis problems (N=29)	2. Severe with cannabis problems (N=174)	3. Severe without alcohol or drug problems (N=226)	4. Moderate with mental health problems (N=156)	5. Moderate without mental health problems (N=95)	Omnibus F / x2	Severe v.s. moderate
Outcome variables							
Internalizing problems at follow up	61.05	64.57[5]	61.67[5]	62.81[5]	40.16[2,3,4]	9.75***	**
Externalizing problems at follow up	63.48[5]	66.67[4,5]	61.71[5]	51.83[2,5]	36.22[1,2,3,4]	17.78***	***
Quality of life at follow up	58.62	58.83[5]	60.66	59.07[5]	63.05[2,4]	2.73*	n.s.
School at follow-up	0.14	0.23	0.15	0.17	0.18	3.48	n.s.
Work at follow-up	0.33	0.32	0.33	0.26	0.32	1.78	n.s.
Violent crimes	0.52	0.30[3,4]	0.19[2]	0.11[2]	0.12	4.74**	***
Sexual crimes	0.03[3,4,5]	0.01	0.00[1]	0.00[1]	0.00[1]	2.96*	n.s.
Property crimes with violence	0.07	0.06	0.06	0.04	0.08	0.36	n.s.
Property crimes without violence	0.76	0.26	0.31	0.17	0.24	3.02*	n.s.
Destruction/public order crimes	0.34	0.20	0.19	0.05	0.08	4.17**	***
Drug crimes	0.10	0.08	0.08	0.13	0.02	1.52	n.s.
Traffic crimes	0.28	0.07	0.09	0.12	0.04	2.07	n.s.
Other crimes	0.41	0.11	0.17	0.12	0.13	3.39**	n.s.

Figure 1. Indicators per cluster (N=680)



Discussion

The current study sought to disentangle multi-problem young adult behavior by using a model-based cluster analysis approach. A five-cluster solution provided a statistically efficient and conceptually helpful way of grouping the study population according to the severity and nature of their problems. Implications of the differences between

the clusters were explored in terms of childhood risk factors, baseline functioning, and outcomes at 14 month follow up.

The major half of the study population (63.1%) scored above the total group mean on indicators of all key life domains, with the exception of cannabis use in cluster 3; these multi-problem young adults constitute the three severe problem clusters. Cannabis and alcohol misuse, or the absence of it, showed to be important distinguishing indicators in the nature of the problems between the three severe problem clusters. Between these groups no significant differences in childhood risk factors and group outcomes were found. However, some of these may be obscured because of the small size of the first cluster (N=29) and the strict correction for multiple testing applied. For example, at follow up the first cluster committed nearly twice as many violent crimes as the second cluster and nearly thrice as many as the third cluster. The alarmingly high levels of cannabis use in cluster 1 and 2, and alcohol use in cluster 1, calls for careful treatment attention to the interplay between multi-problem young adults' problems resulting from substance use and their other existing mental health, social and justice problems. High-risk youth using cannabis as self-medication to cope with negative affect is well documented within the literature (Fox, Towe, Stephens, Walker, & Roffman, 2011; Miller, Chen, & Parker, 2011) and this is likely present in our sample as well. Cognitive-behavioral interventions can be extended with modules concerning drug and alcohol use in which alternative means for dealing with negative affective states are addressed (Marlatt & Gordon, 2005). Furthermore, services to decrease recidivism appear to be most needed for the members of the addiction problem profiles, which is in line with findings from Lee et al. (2017).

The minor half of the study population (36,9%) scored below the total group mean on indicators of all key life domains, with the exception of internalizing problems in cluster 4; they constitute the two moderate problem clusters. Between the moderate groups, differences in childhood risk factors and group outcomes were found, in which the members of the group without mental health problems always struggled less. This cluster seems to be functioning relatively well across all key life domains and reported less childhood adversities and better group outcomes. Whereas the moderate mental health problem group requires mental health care, the group without mental health problems might benefit from more practical oriented intervention approaches in which assistance with issues such as financial management and finding a job is available. Such practical support can be an effective additional rehabilitation component when mental health problems, addiction and antisocial behavior are already under control (MacKenzie & Farrington, 2015). However, most traditional clinical practices treat mental health and substance use problems, but do not yet address the other care needs of multi-problem young adults, such as help with housing, education and employment (Davis & Stoep, 1997). In order to make truly

multimodal interventions for struggling youngsters more available and effective, we first need general consolidation of the idea that our care system must widen its scope beyond providing care for isolated problems. Rather, it needs to treat the complex social, environmental and developmental interplay of adversities that multi-problem young adults encounter.

The three severe groups differed greatly in many aspects from the two moderate groups. They have experienced more ACEs, specifically emotional and physical abuse, and alcohol and drug use in the family. In addition, they currently present with much higher levels of antisocial behavior, most notably in aggression and psychopathic traits. This is also visible from their higher numbers of committed violent crimes. Since the structure of the multi-problem clusters was for an important part based upon the severity of problems, this may speak for the potential benefit of screening early in the process of selecting appropriate intervention procedures and/or treatment programs for multi-problem young adults. In the Netherlands, young adults up to 27 years old can apply for help at municipal social welfare agencies when they experience problems in their key life domains. These institutions use the validated SSM-D (Fassaert et al., 2014; Lauriks et al., 2014) as a decision support tool; professional youth workers score the ability of the individual young adults to provide for themselves regarding key life domains (e.g. mental health, justice, social network and addiction) with or without adequate help from informal or formal care providers. This early-stage, broad screening procedure helps to differentiate between young adults with adequate self-sufficiency and our target population that requires professional support; an extended screening can subsequently be carried out within the multi-problem population to determine their specific treatment needs. Flexible interagency collaboration between municipal social services, multimodal treatment programs, mental health institutions and the criminal justice system is urgently advised to ensure that multi-problem young adults' problem heterogeneity is adequately recognized, diagnosed and effectively treated.

A final, important consideration is the direction of future research: it should aim to study how and when problems in key life domains, as according to ecobiodevelopmental theory (Donovan & Jessor, 1985; Doreleijers et al., 2000; Hawkins, 2009; McPherson et al., 2014), interact with each other. Although our study showed that within a multiproblem group problems concerning the domains of justice, addiction, mental health and social network cluster together and that these clusters are meaningfully different in terms of childhood and context factors, no explications about causality and preferred treatment order of the problems can be made. Since it is now widely acknowledged that human biological, psychological and environmental conditions and problems in key life domains influence each other, the next step in thinking about multi-problem youth behavior is to understand how these adversities interact with human conditions and with each other. A new ecobiodevelopmental

framework within the fields of clinical medicine and public health is syndemics; a promising theoretical approach to measure how social contexts provide opportunities for negative problem/disease interactions to occur and how diseases cluster together within a specific time and place (Singer, Bulled, Ostrach, & Mendenhall, 2017). The syndemic framework might be easily adapted to fit within the fields of developmental psychology and child and adolescent psychiatry.

Limitations

First, this study was exploratory; it aimed to identify latent clusters that exist within our sample. Since a priori hypotheses about the differences between the clusters were not formulated, our findings might be partially dependent on specific sample characteristics. However, as we have a large sample size our sample is likely representative of the population of multi-problem young adults in Rotterdam. Second, although sexual risk behavior is suggested to be an important construct of multi-problem behavior as well (Donovan & Jessor, 1985; Mun et al., 2008), we did not have data to operationalize this construct in the current model. Future research may benefit from investigating the variability of sexual risk behavior within multi-problem populations.

Conclusion

Multi-problem young adult behavior clusters within profiles that differ according to the severity and nature of problems. By pursuing an ecobiodevelopmental policy, by investing in multimodal treatments, and by stimulating interagency collaboration, the cycle of interrelated adversities might be broken so we can help multi-problem young adults stand on their own feet (again).

Chapter 3: Neural correlates of moral evaluation and psychopathic traits in male multi-problem young adults

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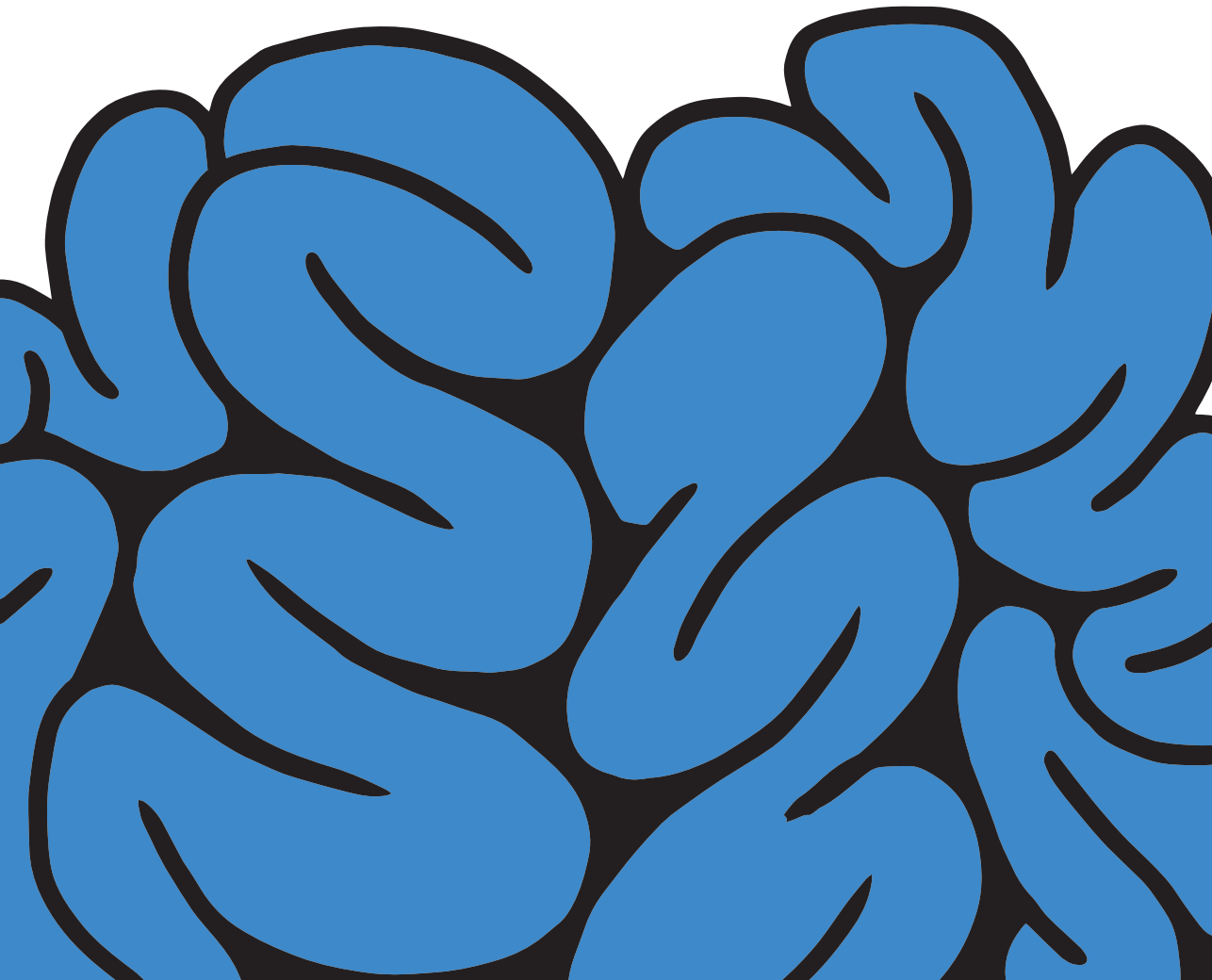

Abstract

Multi-problem young adults (18-27 years) present with a plethora of problems, including varying degrees of psychopathic traits. The amygdala and ventromedial prefrontal cortex (vmPFC) have been implicated in moral dysfunction in psychopathy in adolescents and adults, but no studies have been performed in populations in the transitional period to adulthood. We tested in multi-problem young adults the hypothesis that psychopathic traits are related to amygdala and vmPFC activity during moral evaluation. Additionally, we explored the relation between psychopathic traits and other regions consistently implicated in moral evaluation. Our final sample consisted of 100 multi-problem young adults and 22 healthy controls. During fMRI scanning, participants judged whether pictures showed a moral violation on a 1-4 scale. Whole brain analysis revealed neural correlates of moral evaluation consistent with the literature. Region of interest analyses revealed positive associations between the affective callous-unemotional dimension of psychopathy and activation in the left vmPFC, left superior temporal gyrus, and left cingulate. Our results are consistent with altered vmPFC function during moral evaluation in psychopathy, but we did not find evidence for amygdala involvement. Our findings indicate the affective callous-unemotional trait of psychopathy may be related to widespread altered activation patterns during moral evaluation in multi-problem young adults.

Introduction

Psychopathy is a psychological construct characterized by affective callous-unemotional traits, impulsive and irresponsible behavior, and grandiose-manipulative interpersonal traits (Cooke & Michie, 2001). Individuals with high psychopathic traits engage in morally inappropriate behavior (e.g., committing crimes, lying, and cheating) and show a lack of guilt or remorse after performing antisocial actions (Cleckley, 1941). However, research suggests they are generally capable of differentiating right from wrong when evaluating moral dilemmas or situations (Cima, et al., 2010; Moll et al., 2002) and their moral reasoning can thus prove normal when assessed behaviorally. In the last decade, there has been an increasing interest in the underlying neurobiology of moral reasoning. Clarifying which neural processes are aberrant in persons with psychopathic traits may help understand why individuals with high psychopathic traits engage in their immoral behaviors.

Previous studies have investigated the relationship between psychopathic traits and moral processing in (forensic) adolescents and adults, but as of yet no research has specifically focused on a young adult group (aged 18-27). Given that the transition from adolescence to adulthood (Arnett, 2000) is especially challenging for vulnerable populations (Osgood, Foster, & Courtney, 2010) young adulthood is an important period to study distinctly (Arnett, 2007). In the present study, we investigated a sample of young adults (18-27 years old) who dysfunction in society and suffer from multiple problems. These multi-problem young adults lack a stable income, do not have the prerequisites to get a job, most of them have engaged in criminal activities of ranging seriousness (e.g., from shoplifting to violent crimes), and two thirds of them have had Child Protection Service (CPS) interference, chiefly due to judicial problems before age 18 (van Duin et al., 2017). It is an ecologically valid sample in which antisocial behavior is displayed in varying degrees. Therefore, we expect their psychopathic traits to vary accordingly from very low to very high. We measured psychopathy continuously, which is preferable over a taxonomic approach (Edens et al., 2006; Guay et al., 2007; Murrie et al., 2007) as it allows for the entire range of the construct to be taken into account.

Brain areas that have been implicated in the processing of moral information in healthy populations include the amygdala and ventromedial prefrontal cortex (vmPFC), which are important for processing emotional information; the dorsolateral prefrontal cortex (dlPFC), which is engaged in utilitarian decision making; and the superior temporal gyrus (STG), which is important when thinking about others (Fumagalli & Priori, 2012; Greene et al., 2001; Harenski & Hamann, 2006; Heekeren et al., 2003; Moll et al., 2002). A recent meta-analysis of fMRI research of moral processing (Garrigan et al., 2016) distinguished between studies investigating moral judgments about situations (moral evaluations) and studies requiring participants

to make moral decisions as if they were the actor (moral response decisions), as evidence suggests these are at least partially different processes (Tassy et al., 2013a). The current study focuses on moral evaluations. Six brain areas were found to be specifically involved in making moral evaluations (Garrigan et al., 2016): the right and left STG, the left cingulate gyrus (CG), the right medial frontal gyrus (MFG; part of the vmPFC) and two distinct areas in the left MFG (one in BA9, one in BA10).

It has been argued that amygdala and vmPFC dysfunction lie at the basis of the moral impairments of individuals high in psychopathic traits (Blair, 2007). The amygdala is suggested to aversively reinforce actions that harm others; the vmPFC in turn processes this information and creates an outcome expectancy. When amygdala functioning is disrupted, the vmPFC fails to appropriately represent the valenced information, leading to immoral behavior. To date, decreased amygdala activity during moral processing (immoral minus nonmoral contrasts, where nonmoral stimuli are negative but not immoral) has been found in community volunteers with psychopathic traits (Glenn et al., 2009a), but not in incarcerated males (Harenski et al., 2010), incarcerated adolescents (Harenski et al., 2014a), or incarcerated women (Harenski et al., 2014b). However, in the adolescent and female samples negative correlations between psychopathic traits and amygdaloid brain activity have been observed when contrasting both immoral and nonmoral stimuli with neutral stimuli (which are neither negative nor immoral). Negative correlations between vmPFC activity and psychopathic traits during moral processing have been reported in some studies (Glenn et al., 2009a; Harenski et al., 2010), but not others (Harenski et al., 2014b; Harenski et al., 2014a). In short, although a theoretical basis for amygdala and vmPFC dysfunction underlying moral dysfunction in psychopathy exists (Blair, 2007), neuroimaging results vary depending on samples and different ranges and variation of psychopathic traits within these samples.

As mentioned, in the current study we investigated a sample of multi-problem young adults (18-27 years old) with varying levels of psychopathic traits. At the time of assessment, all participants were enrolled in a day treatment program intended to help reintegrate into society. Within this heterogeneous sample, we employed a task that requires participants to make moral evaluations about situations that are presented as pictures. We included a group of healthy controls primarily to assess whether the task worked appropriately and whether multi-problem young adults are capable of performing the task. We expected to find brain activity related to moral evaluation in line with the current literature (i.e., increased vmPFC, STG, and CG activity), and tested the hypothesis that the three psychopathic dimensions are negatively related to amygdala and vmPFC activity during moral evaluation in multi-problem young adults. We also tested whether psychopathic traits are associated with other regions consistently implicated in moral processing (i.e., STG and CG). We expected the affective callous-unemotional dimension of psychopathy to be

specifically relevant as it is representative of behavior related to moral evaluation (i.e., shallow affect, lack of empathy, lack of remorse). We investigated the impulsive-irresponsible and grandiose-manipulative dimension exploratively.

Method

Participants

Participants were 110 male multi-problem young adults (part of a larger study including 696 multi-problem young adults; Luijks et al., 2017). They were recruited at the start of day treatment program De Nieuwe Kans (DNK; translated as "New Opportunities"). DNK provides a multimodal day treatment program, which aims to increase the self-sufficiency and decrease recidivism of multi-problem young adults. Additionally, 25 age and gender group matched healthy controls were included in the study. Controls were selected to have average education. Exclusion criteria for the fMRI study were non-corrected defective vision and fMRI contra-indications. Ten multi-problem young adults were excluded due to excessive movement (N = 3) or poor task performance (e.g., more than 5 missed trials; N = 7). Three controls were excluded due to poor task performance. The final sample included 100 multi-problem young adults and 22 healthy controls. See table 1 for an overview of the descriptive data.

This study was carried out in accordance with the recommendations of the Medical Ethical Committee of the VU University Medical Center. The protocol was approved by the VU University Medical Center Medical Ethical Committee (registration number 2013.422 - NL46906.029.13). All subjects gave written informed consent in accordance with the Declaration of Helsinki. Participants received a reimbursement of 30 euros for their participation in the fMRI protocol and an EEG protocol, which was administered on another day.

Instruments

Psychopathic traits were assessed using the Youth Psychopathy Inventory – Short Version (van Baardewijk et al., 2010; also validated in young adults; Colins and Andershed, 2015). The YPI-SV is a self-report measure that distinguishes three factors of psychopathy: an affective callous-unemotional factor, a behavioral impulsive-irresponsible factor, and an interpersonal grandiose-manipulative factor. We used the Measurements in the Addictions for Triage and Evaluation Questionnaire (MATE) to assess current and historic drug use. In order to measure intelligence, we used the short form of the Wechsler Adult Intelligence Scale third version (WAIS-III SF) consisting of four subtests (Blyler et al., 2000): digit symbol coding, information, block design, and arithmetic. The WAIS-III-SF was only assessed in the multi-problem group. See table 1 for descriptive data.

Stimuli

Three types of stimuli were used in the experiment: 25 immoral and negative (e.g., a person threatening another person with a knife); 25 non-moral and negative (e.g., people shouting at each other); and 25 neutral (e.g., people sitting next to each other). In order to select the stimuli, we first presented a set of 120 stimuli selected from the International Affective Picture System (IAPS; Lang et al., 2008) (40 of each type as assessed by JZ) to a pilot group of 134 participants via the online tool Mechanical Turk (Paolacci et al., 2010) and asked the participants to rate them on a

Table 1. Participants characteristics

	Multi-problem young adults (N = 100)		Healthy controls (N = 22)		
	M (Range)	SD	M (Range)	SD	p
Age	22.56	2.41	23.19	2.84	.28
IQ	82.98 (60-107)	10.65	.	.	.
YPI-SV total	34.08 (19-68)	7.92	35.5 (25-50)	5.28	.42
YPI-SV affective	10.68 (6-24)	3.53	11.53 (8-16)	2.57	.29
YPI-SV behavioral	12.19 (7-21)	3.1	12.05 (8-18)	2.57	.84
YPI-SV interpersonal	11.21 (6-23)	3.71	11.95 (6-19)	3.23	.39
Cannabis use past 30 days	14.80 (0-30)	13.24	4.18 (0-16)	6.40	< 0.001
Years of regular cannabis use	4.34 (0-14)	3.78	1.30 (0-10)	2.60	< 0.001
Ratings of stimuli					
Neutral	1.12	0.19	1.07	0.16	.25
Nonmoral	2.17	0.65	1.86	0.64	.04
Immoral	3.21	0.41	3.41	0.4	.04
Education					
No secondary education	90%	.	0%	.	.
Secondary education following	0%	.	41%	.	.
Secondary education finished	10%	.	59%	.	.

1-7 scale on their morality, valence, arousal, and complexity. From each category, 25 pictures were chosen in such a way that the immoral and nonmoral pictures matched on valence, arousal, and complexity, but not on morality. In other words, the moral and non-moral stimuli are specifically distinguishable on morality, which allows us to disentangle moral transgression from negative valence. For an overview of the average ratings of the stimuli see table 2.

Table 2. Average ratings of stimuli via Mechanical Turk (N = 134)

	Moral violation	Valence	Arousal	Complexity
Immoral	5.50	1.68	5.11	4.36
Nonmoral	1.94	1.94	4.90	4.13
Neutral	1.03	4.24	2.52	2.45

Procedure & Task

Participants were told they would be shown pictures that might contain moral violations and were instructed to judge whether this was the case or not on a scale from 1 to 4, where 1 indicated that no moral violation was presented in the picture and 4 indicated that a major moral violation was presented in the picture. Participants were asked to consider the morality of the event depicted whilst viewing the picture and to press on the appropriate button after the picture was replaced by a rating scale. Participants were told that there were no right or wrong answers and that we were interested in their personal opinion.

Each trial consisted of a picture being shown for 5 seconds, a rating scale of 1 to 4 being shown for 3 seconds, and a variable inter stimulus interval of 3 – 8 seconds (average 5.5 seconds), introducing jitter into the experimental design. Pictures were presented pseudo randomly, with a maximum of three pictures of the same condition being shown sequentially. Participants performed three practice trials in order to ensure they understood the experiment. The experiment was administered in two sessions (the first with 38 stimuli, the second with 37 stimuli) with a small break in between so that the task would not be too demanding. The task is based on and similar to that used by Harenski and colleagues (2010). We adopted a different response procedure, requiring participants to press one of four buttons whenever they had decided on their answer, rather than pressing one button when the answer they wanted to give was shown on the screen. Also, we introduced jitter by varying the intertrial intervals around a mean value, rather than using three distinct intertrial intervals. The experiment was created and presented with Presentation 17.1 (https://www.neurobs.com/).

MRI data acquisition and analysis

MRI data were collected on a 3T GE Healthcare MRI scanner at Erasmus Medical Center Rotterdam. Structural T1-weighted images were acquired with a fast-spoiled gradient pulse sequence in 180 sequential sagittal (S/I) slices, with a thickness of 1.0 mm. The repetition time (TR) was 6.4 ms, the echo time (TE) 2.8 ms, the flip angle (FA) 12 degrees, the field of view (FOV) 240 mm, and the matrix size 240x240 mm. Blood oxygen level-dependent T2*-weighted images were acquired axially (R/L) with an echo planar imaging gradient echo pulse sequence in 42 slices of 3.5 mm with a slice spacing of 0.5 mm. The TR was 2000ms, the TE 30ms, the FA 80 degrees, the FOV 220 mm, and the matrix size 64x64 mm.

Functional imaging data were analyzed using Statistical Parametric Mapping 12 (SPM12; http://www.fil.ion.ucl.ac.uk/spm/). As preprocessing steps, for each participant functional images were realigned and unwarped, the structural scan was segmented and co-registered to the mean T2*-weighted image. Images were then normalized to the MNI template and smoothed with an 8mm full-width half maximum Gaussian filter. The three conditions were modelled as 5-second events with the standard hemodynamic response function. Six movement parameters were added as covariates of no interest. Our contrast of interest was the immoral > nonmoral contrast, which is expected to be representative of brain activity due to the moral salience of the stimuli, controlled for the (negative) emotional valence of the stimuli.

We defined a priori regions of interest (ROI) based on the most recent meta-analysis concerning the neural correlates of moral decision-making (Garrigan et al., 2016). We limited the ROIs to areas that were found to be consistently active during moral evaluation tasks. The a priori ROIs are the right and left superior temporal gyrus (STG), the left cingulate gyrus (CG), the right vmPFC, and two distinct areas in the left vmPFC (one in BA9, one in BA10). Additionally, we included the right and left amygdala as ROIs since the amygdala has been implicated both theoretically (Blair, 2007) and empirically (Glenn et al., 2009a; Sevinc & Spreng, 2014) to be involved in moral processing and psychopathy. ROIs were created by forming 8mm-radius spheres around the peak coordinates that are reported in the literature (Garrigan et al., 2016; Sevinc & Spreng, 2014). For the creation of the ROIs and the extraction of the ROI data we used the Marsbar toolbox for SPM (http://marsbar.sourceforge.net/).

In order to compare the ratings of the three picture types between each other and between the multi-problem group and the control group, we performed a repeated measures ANOVA with group as between subjects factor and paired-sample t-tests. To investigate the relationship with IQ in the multi-problem group we performed Pearson's correlations between psychopathy, IQ, and behavioral responses. For the association between psychopathy and ROI-activity during moral evaluation in the multi-problem group, we performed multiple linear regression analyses using

the total psychopathy score or psychopathy subscale scores as independent variables and the extracted ROI data as dependent variables. We performed the analyses with and without IQ and drug use as covariates. Cannabis was the only drug prevalent enough in our sample to take into account (see table 1), we controlled for both recent cannabis use (past 30 days) and historic cannabis use (amount of years that the drug was used at least once per week).

Results

Behavioral results

We compared the ratings of the three picture types between each other and between groups. A repeated measures ANOVA with picture type as within subjects factor and group as between subjects factor showed that the three types of pictures were rated differently in terms of moral violations across all participants ($F(2,240) = 530.52$, $p < .001$). Immoral pictures ($M = 3.25$, $SD = 0.42$) were rated as greater moral violations than nonmoral pictures ($M = 2.11$, $SD = 0.65$; $t(121) = 18.02$, $p < .001$) and neutral pictures ($M = 1.1$, $SD = 0.19$; $t(121) = 52.34$, $p < .001$). Nonmoral pictures were rated as greater violations than neutral pictures ($M = 1.11$, $SD = 0.19$; $t(121) = 18.14$, $p < .001$). There was no main effect of group ($p > .05$), but we found a significant interaction between picture type and group ($F(6.84, 240) = 6.84$, $p < .001$). Multi-problem young adults judged immoral pictures to represent smaller violations ($M = 3.21$, $SD = 0.41$) than controls did ($M = 3.41$, $SD = 0.40$; $t(120) = -2.10$, $p < .05$). In contrast, multi-problem young adults judged nonmoral pictures to represent larger violations ($M = 2.17$, $SD = 0.65$) than controls did ($M = 1.86$, $SD = 0.64$; $t(120) = 2.00$, $p < .05$). Both groups rated the neutral pictures similarly ($p > .05$). See table 1 for an overview.

Within the multi-problem group, none of the ratings of picture types were significantly related to total psychopathy score and psychopathic traits (all ps > .05). We found a negative correlation between IQ and rating of the nonmoral stimuli ($r = -.41$, $p < .001$) thus multi-problem young adults with lower IQs judged nonmoral stimuli to show larger moral violations. IQ was not significantly related to the ratings of immoral ($r = .08$, $p = .41$) and neutral stimuli ($r = -.17$, $p = .11$).

Imaging results

First, we performed a whole brain analysis of the contrast of interest moral > nonmoral across all participants. This revealed significant increased hemodynamic responses in the STG, in several distinct areas of the vmPFC, in the precuneus, the parahippocampal gyrus, in the middle occipital gyrus (MOG), and in the cerebellum (see figure 1).

Also, we found increased activation in the precentral gyrus and the thalamus, this is likely due to the setup of the task: when participants evaluated pictures as not representative of a moral violation or as representative of a slight moral violation they used their left hand, when participants evaluated pictures as representative of a somewhat immoral violation or a strong moral violation participants used their right hand (see table 3 for an overview). No significant differences in activation patterns in any of the brain regions were found between the experimental group and the control group in the analyses of this contrast.

Second, we extracted the summary time courses for the a priori defined ROIs and performed linear regression analyses to examine the relationship between the level of psychopathy and brain activity of the immoral > nonmoral contrast in the multi-problem group. We found the total psychopathy score to be positively related to brain activation in the left vmPFC (BA10) (β = 0.22, $p < .05$) and the left STG (β =

Table 3. fMRI whole brain analysis (immoral > nonmoral), N = 122

cluster-level p(FWE)	k	peak-level p(FWE)	T	x {mm}	y {mm}	z {mm}	Peak coordinate
0.000	2,856	-	17.41	48	-58	12	STG
0.000	2,310	-	17.10	-48	-70	6	MOG
		0.000	7.34	-58	-38	24	
0.000	3,394	-	11.48	4	-56	40	Precuneus
		-	9.70	4	-56	26	
		0.000	7.93	20	-54	14	
0.000	549	-	9.69	18	-52	-24	Cerebellum
0.001	157	0.000	7.15	22	-32	-18	Parahippocampal gyrus
		0.002	5.43	28	-20	-18	
0.004	79	0.000	6.22	16	-62	-48	Cerebellum
0.000	495	0.000	6.17	4	56	20	vmPFC
		0.000	6.08	4	56	-10	
		0.000	5.74	4	64	14	
0.008	48	0.002	5.41	40	4	44	vmPFC
0.014	26	0.006	5.06	26	26	42	vmPFC

0.23, p < .05). We found no significant relation in the other regions of interest. We performed hierarchical regression analyses adding one subscale of the YPI at each level in order to assess their individual contributions to the models. We found the affective callous-unemotional factor score of psychopathy to be positively related to brain activation in the left vmPFC (BA10) (β = 0.23, p < .05), left STG (β = 0.27, p < .01), and CG (β = 0.21, p < .05), see figure 2. The behavioral and interpersonal factors did not predict brain activity in any of the ROIs. See table 4 for an overview.

Third, we added IQ and drug use as covariates in the models. This did not change any of the reported results, but IQ itself was positively related to brain activity in the left vmPFC (BA10; β = 0.18, p < .05), left STG (β = 0.20, p < .05), and left CG (β = 0.20, p < .05).

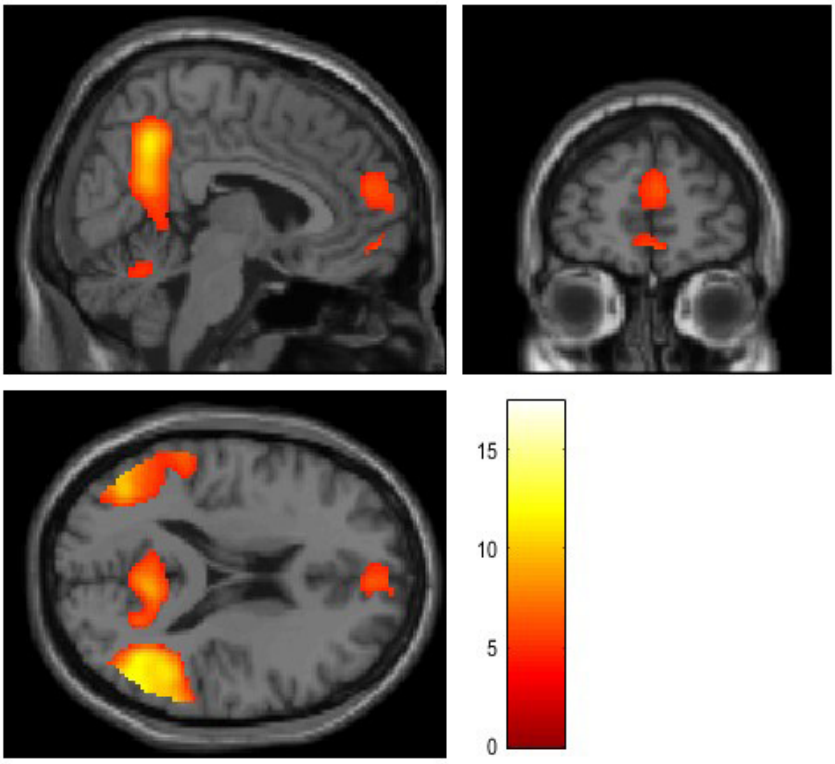

Figure 1. Whole brain analysis of the immoral > nonmoral contrast (x = 6, y = 56, z = 19)

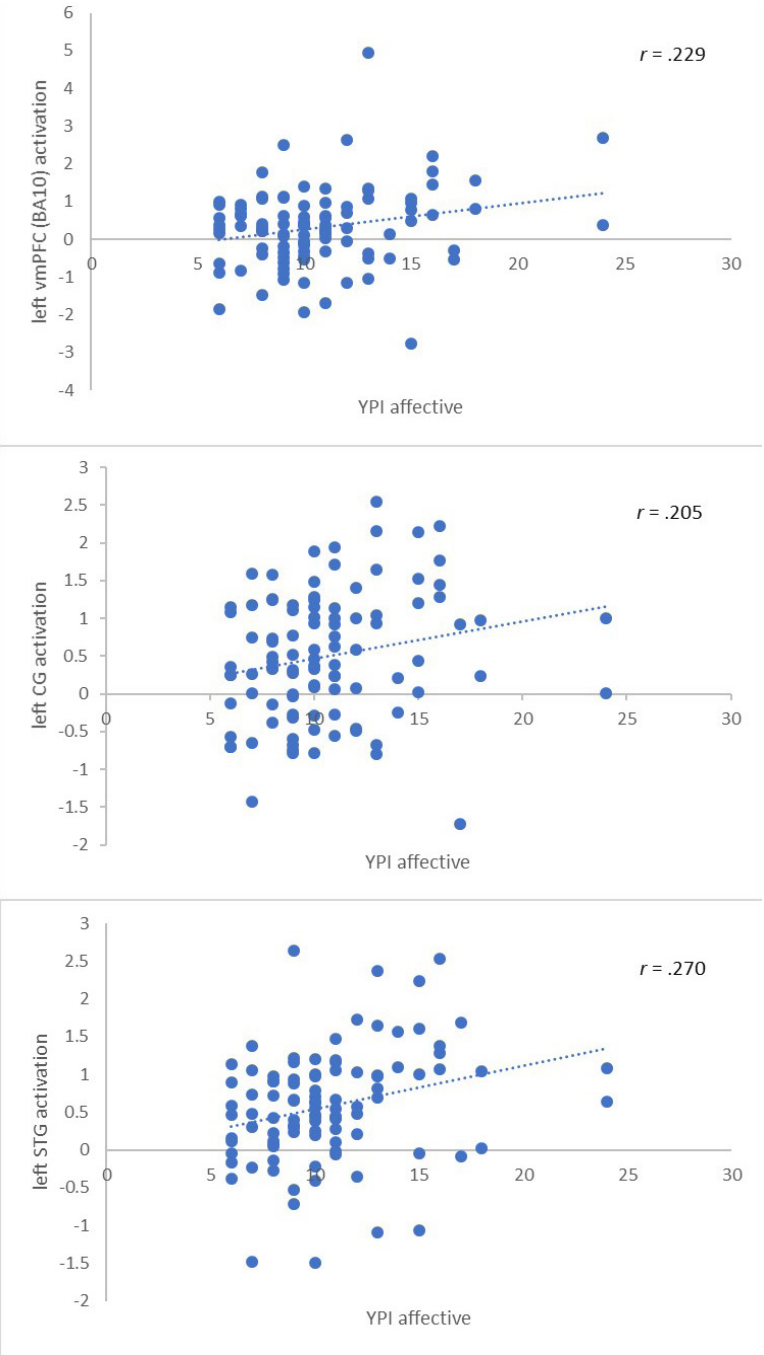

Figure 2. Significant associations between the callous-unemotional affective trait of psychopathy and brain activity in a priori ROIs

Discussion

In this study, we investigated the relationship between psychopathic traits and the neural correlates of moral evaluation in a sample of male multi-problem young adults. Multi-problem young adults were able to discriminate between immoral and nonmoral stimuli, but less well so than the control group, as they gave nonmoral pictures higher moral ratings and immoral pictures lower ratings. In line with previous research, several specific brain regions showed increased activity during moral evaluation, most notably the vmPFC, STG, parahippocampal gyrus, and precuneus. We did not find any negative relationships between the brain activity in these regions and psychopathic traits in the amygdala and vmPFC. Rather, we found no effect in the amygdala and found positive associations in the left vmPFC, left STG, and left CG, indicating that multi-problem young adults high in psychopathic traits show a greater increase in brain activity in these areas during moral evaluation than multi-problem young adults low in psychopathic traits.

Table 4. Regression analyses on extracted a priori ROI summary time courses, N = 100.

Predictor	Outcome	R^2	p
Total psychopathy score	vmPFC L (BA10)	.048	.028
	CG L	.029	.092
	STG L	.052	.022
	vmPFC R	.028	.099
	vmPFC L (BA9)	.011	.300
	STG R	.009	.347
	Amygdala L	.006	.461
	Amygdala R	.000	.910
Affective callous-unemotional score	vmPFC L (BA10)	.053	.022
	CG L	.042	.041
	STG L	.073	.007
	vmPFC R	.036	.057
	vmPFC L (BA9)	.012	.287
	STG R	.009	.354
	Amygdala L	.004	.552
	Amygdala R	.000	.862

Note. The behavioral and interpersonal traits of psychopathy were not significantly related to brain activity in the a priori ROIs.

Multi-problem young adults discriminated less between immoral and nonmoral stimuli than the control group. This difference does not seem to be driven by psychopathic traits, as both groups have similar psychopathic trait scores, and we found no relation between psychopathic traits and participants' responses to the stimuli. Potentially, this finding might be due to a difference in intelligence between groups. Although we did not formally assess the IQ of the control group, we can assume they have a higher level of intelligence than the multi-problem young adults given the low average IQ (mean IQ 83) and lower educational level of the multi-problem young adults. Furthermore, within the multi-problem group there was a moderately strong and negative correlation ($r = -.41$) between IQ and the rating of the nonmoral pictures. It could be the case that individuals with lower IQs are less capable of separating negative situations from immoral situations or that they tend to overinterpret the information shown to them (e.g., if people are shouting, someone must have done something wrong).

The lack of amygdala activity across both groups for the immoral > nonmoral contrast as well as the lack of relation between amygdala activity and psychopathy scores may indicate that amygdala dysfunction in psychopathy might not be specifically relevant to moral evaluations, nor to moral evaluation in general. There is strong evidence for amygdala dysfunction in emotion processing in psychopathy (e.g., Birbaumer et al., 2005; Contreras-Rodríguez et al., 2014; Kiehl et al., 2001; Marsh et al., 2013), but the evidence for a relation with moral processing is less clear. For example, negative relations between amygdala activity and psychopathy have mostly been found in immoral + nonmoral > neutral, immoral > neutral, and nonmoral > neutral contrasts, but not in immoral > nonmoral contrasts (Harenski et al., 2014b; Harenski et al., 2014a). This would also explain why Glenn et al. (2009a) did find an effect in the amygdala as in their analysis they specifically contrasted "moral personal emotion-provoking" and "moral impersonal less emotional" dilemmas. Additionally, a recent and specific meta-analysis on moral processing found no evidence for amygdala involvement (Garrigan et al., 2016) in contrast to an older meta-analysis (Bzdok et al., 2012).

In the vmPFC, we observed a positive relationship between psychopathic traits and brain activity during moral evaluation, indicating that young adults high in psychopathic traits show a greater increase in vmPFC activity during moral evaluation than young adults low in psychopathic traits. One possible explanation is that individuals high in psychopathic traits have to recruit this region to a greater extent in order to reach a normal level of moral evaluation. In fact, studies have shown increased prefrontal brain activity in criminal psychopaths during emotion processing (Kiehl et al., 2001), increased dorsolateral prefrontal brain activity in community volunteers with high psychopathic traits during moral processing (Glenn et al., 2009b), and the affective trait of psychopathy has been found to be positively

related to frontal brain activity when viewing fearful faces (Contreras-Rodríguez et al., 2014). Likewise, in a study in healthy participants, participants with lower moral judgment competence showed increased vmPFC activity during a moral evaluation task compared to participants with higher moral judgment competence scores. In this study, participants performing worse showed increased rather than decreased brain activity (Prehn et al., 2008). That such a mechanism of overcompensation is present in our sample and not in most studies on psychopathic traits and moral evaluation may be due to the specific age range of our sample or its low IQ. Whereas in other studies participants usually have average to high IQs, the average IQ within our sample is low and the variation is limited, it may be the case that a combination of high psychopathic traits and low IQ required multi-problem young adults to engage more brain activity in order to perform the task. Another explanation for the association is that as the vmPFC is a large brain area, distinct areas within the vmPFC may perform different functions when making moral evaluations. Therefore, generalizing activity from specific clusters across the vmPFC may not be prudent and future research disentangling distinct areas functioning within the vmPFC is needed to elucidate this.

In addition to the effects observed in the vmPFC, we found positive relations of similar strength between psychopathic traits and brain activity during moral evaluating in the left CG and the left STG. In accordance with our vmPFC finding, the callous-unemotional affective factor of psychopathy accounted for these observations. A previous studies also reported a negative correlation between moral CG activity and psychopathic traits (Glenn et al., 2009a) but no correlations between moral STG activity and psychopathic traits. However, a negative correlation in the STG has been observed using an immoral + nonmoral > neutral contrast (Harenski et al., 2014b). As we included the CG and STG as ROIs, our analysis is more sensitive to effects in these areas and other studies may have missed these. Our results suggest that most of the brain regions associated with moral evaluating behave aberrantly in psychopathy, rather than the vmPFC and possibly amygdala specifically.

As the effects we observed are all specific to the callous-unemotional affective trait of psychopathy, this is likely the main factor related to moral evaluation in our population. This does not seem surprising since moral evaluating requires empathy to assess a situation, whereas for example impulsivity and grandiosity may be more relevant when deciding what to do. It is possible that deficits in moral evaluation are driven by the callous-unemotional affective trait, whereas deficits in moral response decisions may also be driven by the impulsive and irresponsible behavioral, and grandiose-manipulative interpersonal traits. One study has shown psychopathic traits in a healthy sample to be related behaviorally to moral decisions, but not moral judgment (Tassy et al., 2013b). It would be valuable for future research to delve into the neurobiological differences between moral evaluations and moral response decisions, and investigate whether distinct psychopathic traits are differentially

related to these processes.

A limiting factor in comparing our study to others is the fact that we used the YPI, which is a self-report questionnaire, to assess psychopathy rather than the more extensive PCL-R or PCL-YV (Hare, 2003). The YPI has good convergent validity (Colins & Andershed, 2015) and the YPI and the PCL-YV correlate with moderate strength (Andershed et al., 2007), so it seems unlikely the positive relation between psychopathy and brain activity during moral evaluations is due to the use of a self-report measure. However, other research has suggested that psychopathy subscales specifically are not interchangeable between different assessment instruments (Fink, Tant, Tremba, & Kiehl, 2012), so caution is warranted. Another limitation is that we did not use urine screens or breathalyzer to objectively assess whether participants adhered to the instruction to refrain from substance use prior to the MRI session, all participants reported adhering to the instructions.

In conclusion, we found brain activation related to moral evaluation in the STG, in several distinct areas of the vmPFC, in the precuneus, the parahippocampal gyrus, the middle occipital gyrus (MOG), and in the cerebellum in a group of multi-problem young adults and healthy controls; we found that brain activity in the left vmPFC, left STG, and left CG was associated with the affective callous-unemotional traits of psychopathy; and we found that IQ, but not psychopathic traits are related to the moral evaluations of participants. Our results add to the evidence that brain dysfunction underlies psychopathic traits in moral evaluation and suggest that most of the brain regions associated with moral evaluating are affected in young adults with higher levels of psychopathy, specifically on the affective callous-unemotional dimension, rather than the vmPFC and possibly amygdala alone.

Chapter 4: Error-related brain activity in relation to psychopathic traits in multi-problem young adults: an ERP study

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Abstract

One of the most prominent issues in psychopathy is the inability to adequately monitor one's performance and learn from one's mistakes. We investigated the relationship between psychopathic traits, as measured with the Youth Psychopathy Inventory – Short Version, and both early and late error-related brain activity in an at-risk sample of male young adults. These multi-problem young adults (age 18-27) are severely dysfunctional in society and suffer from multiple problems including financial problems, delinquency, psychological problems, and drug use. Our final sample consisted of 115 multi-problem young adults and 26 controls. Participants performed an Eriksen-Flanker task during EEG measurements. We used the difference wave of the error-related negativity (ΔERN) as a measure of early error processing and the error positivity (Pe) as a measure of late error processing. Multi-problem young adults showed reduced ERN amplitudes compared to controls, but did not differ in Pe amplitude. We found no statistically significant relation between psychopathic traits and ERN and Pe amplitudes within the multi-problem group. Thus, we found evidence for dysfunctional error-processing in multi-problem young adults compared to controls. However, within the multi-problem sample we did not find evidence for a relationship between psychopathic traits and dysfunctional error-processing. One explanation may be that this is due to the specific developmental stage of our young adult participants in which a transition between error-processing deficits, as present in adolescents high in psychopathic traits, and error-processing overcompensation, as present in adults high in psychopathic traits, may occur.

Introduction

Psychopathy is a personality disorder characterized by affective callous-unemotional traits, impulsive and irresponsible behavior, and grandiose-manipulative interpersonal traits, with antisocial behavior either included in its definition (Hare & Neumann, 2008) or viewed as a consequence (Cooke & Michie, 2001). Psychopathic traits are related to a plethora of problems, both affective and cognitive. One of the major issues is the failure to adapt behavior to changing or new situations (e.g., to learn from mistakes). For instance, individuals with high psychopathy scores show impaired passive avoidance learning (Newman & Kosson, 1986), impaired reversal learning (Budhani, Richell, & Blair, 2006), and impaired fear conditioning (Birbaumer et al., 2005). A prerequisite for behavioral adaptation is the ability to monitor one's own performance, which is reduced in psychopathy and helps explain these behavioral deficits (Schulreich, 2016). An essential part of performance monitoring is the ability to process error-related information and when this is reduced, individuals may fail to adequately adapt their behavior.

So far, most studies on the association between error processing and psychopathy have focused on samples high in psychopathic traits, specifically in adolescent and adult incarcerated populations. Lately, more attention in forensic research is drawn to antisocial young adults and their specific needs for treatment and intervention. Since young adulthood is now regarded as a developmental stage distinct from adolescence in which both neurobiological and psychosocial changes occur (Arnett, 2000) it may prove useful to study error processing within dysfunctional populations who are challenged in making a successful transition to adulthood (Osgood et al., 2010). Multi-problem young adults (18-27 years old) are such a population: they lack a stable income, do not have the prerequisites to get a job, often show serious psychological dysfunction and drug use, most of them have engaged in criminal activities of ranging seriousness (e.g., from shoplifting to violent crimes), and two thirds of them have had Child Protection Service (CPS) interference, chiefly due to juvenile delinquency and experienced maltreatment (van Duin et al., 2017). In view of the heterogeneity of their problems, we expect their psychopathic traits to vary from very low to very high. As psychopathy is better represented dimensionally than taxonomically (Edens et al., 2006; Guay et al., 2007; Murrie et al., 2007), in order to improve theoretical embedding it is particularly useful to study it as a dimensional construct.

Because error processing is a fast process, it is often investigated using event-related potentials (ERPs) in the electroencephalogram (EEG). Due to the high temporal resolution, it can adequately measure rapid brain processing of errors. The main components of interest are the error-related negativity (ERN) and the error positivity (Pe). The ERN occurs within approximately 100 ms after an error has been

made (Holroyd & Coles, 2002) and is thought to represent the early, automatic, and unconscious processing of an error (Bernstein, Scheffers, & Coles, 1995), whereas the Pe occurs between approximately 200 to 400 ms after an error has been made (Falkenstein, Hohnsbein, Hoormann, & Blanke, 1990) and is thought to represent a conscious and more elaborate, late processing of an error (Ullsperger et al., 2010). Evidence from source localization (Dehaene & Tucker, 1994; van Veen & Carter, 2002) and fMRI studies (Edwards, Calhoun, & Kiehl, 2012; see Ridderinkhof, Ullsperger, & Crone, 2004) both indicate that the ERN and Pe are generated by the anterior cingulate cortex, which in turn is theorized to play an important role in problems with motivation and regulation of behavior in psychopathy (Koenigs, 2012). However, literature suggests that early and late error processing are related to psychopathic traits differently.

Previous studies on early error-processing (as measured with the ERN) in community samples have found some associations between the ERN and psychopathy, but findings have been quite diverse. In a task involving pleasant, neutral, aversive, and non-words, one study found impulsive psychopathic traits to be related to a smaller ERN (Heritage & Benning, 2013). Similarly, impulsive psychopathic traits have been associated with a reduced ERN in a neutral task (Bresin et al., 2014; Pasion et al., 2016). However, other findings in neutral tasks point to a relation between interpersonal traits and an increased ERN (Pasion et al., 2016), no association between affective psychopathic traits and the ERN (Bresin et al., 2014), and low-socialized students having smaller ERNs during punishment than reward conditions (Dikman & Allen, 2000). Within antisocial samples, findings have fairly consistently failed to observe a significant relationship between psychopathy scores and ERN amplitude. Studies in violent adult male offenders (Brazil et al., 2009; Steele, Maurer, et al., 2015), psychopathic patients (Brazil et al., 2011), incarcerated adolescents (Maurer et al., 2015, 2018), and incarcerated female offenders (Maurer et al., 2016) found no evidence for a relationship between psychopathic traits and ERN abnormalities. All these studies used cognitive tasks (either a Go Nogo task or a Flanker task) without affective components. One earlier study also did not find any relation between psychopathic traits and the ERN in a letter Flanker task, but did find that violent offenders showed a reduced ERN compared to healthy controls in an affective Flanker task employing angry and fearful faces as stimuli (Munro et al., 2007), suggesting early error processing may be impaired when specifically processing affective information. One study did find a reduced ERN in psychopathic individuals compared to controls in a reinforcement learning task (von Borries et al., 2010). Thus, although in community samples findings have been inconsistent, in antisocial samples psychopathic traits seem to be unrelated to the ERN during affectively neutral tasks, suggesting general early error processing is likely intact in psychopathy.

In contrast, previous research has provided evidence for dysfunctional late

error processing (as measured with the Pe) in relation to psychopathic traits, but the results have been less consistent than for early error processing. Most studies have found a negative relation between psychopathic traits and the Pe, indicating that psychopathy is associated with reduced late error processing. These include studies in violent adult male offenders (Brazil et al., 2009), in incarcerated adolescents (Maurer et al., 2015), and in incarcerated female offenders (Maurer et al., 2016). However, Munro and colleagues (2007) found no difference between violent offenders and healthy controls on the Pe in neither a letter Flanker nor an affective face Flanker task and no relation between Pe and psychopathic traits was found in a community sample (Heritage & Benning, 2013). Likewise, in incarcerated adolescents no relation between Pe and self-reported psychopathic traits was found (Maurer et al., 2018). Lastly, Steele and colleagues (2015) found an opposite relation between psychopathic traits and the Pe, indicating that offenders with higher psychopathic traits had an increased Pe, and later showed this increased late error processing to also be predictive of rearrest (Steele et al., 2015). In short, dysfunctions in the later stage of error processing do seem to be present in psychopathy, but it remains unclear why the direction of the relation differs between samples. Another unsolved question is which specific psychopathic factors (i.e., grandiose manipulative, callous unemotional, and impulsive irresponsible) contribute in what way to the relationship with error processing. Older studies did not differentiate between factors (Brazil et al., 2009; Munro et al., 2007) and more recent studies have not consistently found the same factor to be of relevance (Maurer et al., 2015; Maurer et al., 2016; Steele et al., 2015).

Where other studies focused on adolescents or adults, here we aim to extend these results in a sample of young adults (18-27 years old) who are severely dysfunctional in society and suffer from multiple problems including financial problems, a low educational level, criminal activities of ranging seriousness (e.g., from shoplifting to violent crimes), psychological problems, and drug use (van Duin et al., 2017). To our knowledge, this is the first study to investigate psychopathic traits and error processing in a large sample of dysfunctional individuals in this specific developmental stage. Within this sample, we employed a letter Flanker task, similar to previous studies (Brazil et al., 2009; Munro et al., 2007). We included a group of healthy controls to assess whether the task worked appropriately and to investigate whether multi-problem young adults as a group perform differently compared to a healthy population. The inclusion of the three psychopathic factors as distinct predictors allows for investigation of possible differential associations between the separate factors and error processing. Based on previous findings, we expected to find no association between psychopathic factors and early error processing (ERN) and tested the hypothesis that the three psychopathic dimensions are related to late error processing (Pe) in multi-problem young adults. Specifically, we expected the

total psychopathy score to be negatively related to Pe amplitude. As findings on the specific factors are scarce and inconsistent, we formulated no specific hypotheses on which psychopathic factor(s) could drive the effect. Studying these associations may prove useful in the prospective possibility of targeting error-related brain activity as a relevant process for intervention, as it is related to criminal recidivism (Aharoni et al., 2013) and seems to be changeable in both healthy controls (Larson, Steffen, & Primosch, 2013) and psychopaths (Konicar et al., 2015). However, before error-related brain activity can possibly be used for intervening on an individual level, more knowledge on the robustness of the association between psychopathy and error processing in specific samples is first necessary.

Methods and materials

Participants

Participants were 127 male multi-problem young adults (age 18-27), recruited at the start of day treatment program De Nieuwe Kans (DNK; translated as "New Opportunities"). DNK provides a multimodal day treatment program for multi-problem young adults with a history of delinquency (81% had a criminal record) and Child Protective Services contact (65%), financial problems, a low educational level, and drug use (53% has regularly used cannabis for at least 5 years). Young adults are referred to DNK by youth care, probation services, mental health services, municipal or social organizations, and can also sign up themselves. This program employs cognitive behavioral techniques and rehabilitation components, such as cognitive skills training, drug treatment, and education (Luijks et al., 2017). The current study is part of a larger cohort study which includes 696 multi-problem young adults. Additionally, 27 age and gender group matched healthy controls were included in the present study. Controls were selected to be following or have finished secondary education. Six multi-problem young adults were excluded because they felt the task took too long and failed to complete it, six multi-problem young adults and one control subject were excluded because less than six error trials were usable for analysis (Olvet & Hajcak, 2009). The final sample included 115 multi-problem young adults and 26 healthy controls.

All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. The study has been approved by the Medical Ethical Committee of the VU University Medical Center (registration number 2013.422 - NL46906.029.13) and all participants provided written informed consent. Participants

received a reimbursement of 30 euros for their participation in the EEG protocol and an fMRI protocol, which was administered on another day.

Table 1. Participant characteristics

	Multi-problem young adults (N = 115)		Healthy controls (N = 26)		
	M	SD	M	SD	p
Age (years)	22.46	2.32	23.10	2.60	.216
IQ	82.29	10.12	.	.	.
Education					
No secondary education	93%	.	0%	.	.
Secondary education following	0%	.	42%	.	.
Secondary education finished	7%	.	58%	.	.
Questionnaires					
YPI-SV interpersonal	11.33	3.84	13.20	3.75	.028
YPI-SV affective	10.74	3.53	11.56	3.11	.287
YPI-SV behavioral	12.21	3.14	11.88	2.64	.624
YPI-SV total	34.28	8.12	36.64	6.15	.174
Cannabis use past 30 days	14.14	13.38	3.92	6.14	<.001
Years of regular cannabis use	4.25	3.73	1.17	2.41	<.001
Error processing					
ΔERN (μV)	-4.94	4.75	-7.55	5.02	.013
ΔPe (μV)	5.90	5.08	7.42	5.08	.169
Accuracy	.81	.16	.87	.09	.015
Reaction time (ms)	441.39	77.03	447.45	46.57	.701
Congruency effect	.13	.15	.16	.11	.381
Correctness effect (ms)	45.19	30.77	41.74	28.20	.601
Post-error slowing (ms)	41.44	39.35	45.14	30.14	.837

Instruments

As a measure of psychopathic traits, we employed the Youth Psychopathy Inventory – Short Version (van Baardewijk et al., 2010). The YPI-SV is a self-report measure that distinguishes three factors of psychopathy: an affective callous-unemotional factor, a behavioral impulsive-irresponsible factor, and an interpersonal grandiose-manipulative factor. It has been validated in young adults (Colins & Andershed, 2015). We used the Measurements in the Addictions for Triage and Evaluation Questionnaire (MATE) to assess current and historic drug use. In order to measure intelligence, we

used the short form of the Wechsler Adult Intelligence Scale third version (WAIS-III SF) consisting of four subtests (Blyler et al., 2000a): digit symbol coding, information, block design, and arithmetic. The WAIS-III-SF was only assessed in the multi-problem group.

Task & Procedure

The Eriksen Flanker task was employed to measure error processing (Eriksen & Eriksen, 1974) during EEG measurement. Stimuli were four letter strings (HHHHH, SSSSS, HHSHH, SSHSS) presented on a monitor placed 150 cm away from the participant. Participants were required to respond to the middle letter. They responded by pressing on a button on a response box with their left index finger when the middle letter was an S and their right index finger when the middle letter was an H. Each trial consisted of (1) a fixation cue for 150ms, (2) one of the letter-string stimuli for 52ms, (3) a blank screen for 648ms, and (4) a feedback symbol for 500ms which indicated whether the given response was correct (+), incorrect (-), or too late (!). Responses were defined as too late when they were given later than 700ms after stimulus onset. We used an intertrial interval of 100ms. Thus, one trial lasted for 1450ms. The entire task lasted for 9 minutes and 40 seconds and was performed in five blocks in between which participants could take a break for as long as they wanted. The task is identical to that used by (Marhe, van de Wetering, & Franken, 2013).

The measurements were performed in the Erasmus Behavioral Lab of the Institute for Psychology at the Erasmus University Rotterdam. Participants were seated in a comfortable chair in a sound-attenuated room with dimmed lights. A trained researcher explained the task, followed by a practice run consisting of eight trials. In total, five blocks of 80 trials were administered and participants could take breaks for as long as they liked in between the blocks.

EEG recording and processing

We used a Biosemi ActiveTwo System amplifier to measure brain activity with EEG from 32 scalp sites and one additional scalp sites (FCz). Silver chloride (Ag/AgCl) electrodes were placed upon the scalp according to the 10-20 International System. Two electrodes were placed on the left and right mastoids to record reference activity. Two electrodes were placed below and above the left eye to measure the vertical electro-oculogram (VEOG) and two electrodes were placed at the outer canthi of both eyes to measure the horizontal electro-oculogram (HEOG). Signals were digitized with a sampling rate of 512Hz and 24-bit analogue-to-digital conversion, and filtered offline. Data were filtered using a low cutoff of 0.15Hz and a high cutoff of 30Hz (24dB/octave slope). Data were segmented into 1100ms epochs (500ms pre-response to 600ms post-response). Ocular artifacts were corrected using the Gratton and Coles

algorithm (Gratton, Coles, & Donchin, 1983). The -100ms to 0ms pre-response period was used as baseline. Additional artifact rejection was performed automatically. We employed a minimum amplitude of -100μV and a maximum amplitude of +100μV.

Data analysis

For the behavioral data (accuracies, reaction times), we used mixed ANOVAs to investigate basic task effects (congruency on accuracy, correctness on reaction time, and post-error slowing; PES) and whether these differ between groups. For other measures, we performed independent sample t-tests with group as independent variable to compare the multi-problem group with the healthy control group. We used Pearson correlations to investigate the relation between behavioral measures, covariates (age, IQ, and drug use) and psychopathic traits within the multi-problem group.

ERPs were quantified by averaging the mean amplitudes in a specific time window across a response condition (correct or incorrect). For the ERN we used a time window of 25-100ms post-response (Marhe et al., 2013a) on the FCz electrode where amplitudes were highest, for the Pe we used a time window of 250-400ms post-response (Brazil et al., 2009) on the Cz electrode where amplitudes were highest. We performed a 2x2 mixed ANOVAs with response condition (correct vs. incorrect) as within subject factor and group (multiproblem young adult vs. control) as between subject factor to assess whether expected differences between correct and incorrect trials occurred and whether these differences varied with group (response condition x group interaction). Finally, hierarchical multiple linear regression analyses were used to examine associations between distinct psychopathic traits and error-related brain activity. Analyses were performed on the ERN difference wave (ΔERN) to isolate variation related to performance monitoring (Luck, 2014). We calculated difference waves by subtracting the mean amplitudes for the correct trials from the mean amplitudes for the incorrect trials for each participant. As the ERN is a negative peak, a more negative difference wave indicates increased early error-related brain processing. For the Pe, a more positive amplitude indicates increased later stage error-related brain processing.

Results

YPI validation

Unexpectedly, the multi-problem young adults scored slightly lower on the grandiose-manipulative interpersonal trait of psychopathy than the controls (M = 11.33 vs. 13.20), whereas they scored similar to the controls on the affective callous-unemotional trait

(M = 10.74 vs. 11.56), the impulsive-irresponsible behavioral trait (M = 12.21 vs. 11.88), and the total score (M = 34.28 vs. 36.64; see table 1). Possibly, this is a chance finding that has no consequences for our analysis as we are interested in psychopathic traits within the experimental group. Nonetheless, to ensure the validity of the YPI in our sample, we investigated internal validity by checking Cronbach's alpha for each subscale. For the interpersonal factor $\alpha = .76$, for the affective factor $\alpha = .65$, for the behavioral factor $\alpha = .70$, and for the total score $\alpha = .80$. These figures are consistent with the literature (Colins & Andershed, 2015). Moreover, to ensure criterion validity of the YPI in our sample we performed correlation analyses between the YPI subscales and relevant external criterium constructs: reactive aggression, proactive aggression, current cannabis use, and lifetime cannabis use. For the interpersonal factor we found positive correlations with both proactive ($r = .20$, $p < .05$) and reactive ($r = .39$, $p < .001$) aggression. For the affective factor we found positive correlations with both proactive ($r = .19$, $p < .05$) and reactive ($r = .30$, $p < .01$) aggression. For the behavioral factor we found positive correlations with both proactive ($r = .42$, $p < .001$) and reactive ($r = .44$, $p < .001$) aggression, as well as recent ($r = .20$, $p < .05$) and lifetime ($r = .20$, $p < .05$) cannabis use. Finally, we performed a confirmatory factor analysis on the three-factor structure of the YPI using the lavaan package in R (Rosseel, 2012). The RMSEA and CFI indices for the three-factor model were .05 and .90, consistent with the literature (Colins & Andershed, 2015). Together, these findings indicate that the YPI is a valid instrument in our sample.

Behavioral results

We tested whether the task elicited the expected pattern of basic effects. Mixed ANOVAs revealed main effects of congruency on accuracy ($F = 88.09$, $p < .001$) with congruent stimuli being more accurately responded to (89%) than incongruent stimuli (75%); a main effect of correctness on reaction time ($F = 174.29$, $p < .001$) with incorrect trials being reacted to quicker (M = 406.07ms) than correct trials (M = 450.62ms); and a main effect of post error slowing ($F = 139.00$, $p < .001$) with post-error trials being responded to slower (M = 449.83ms) than other trials (M = 406.08ms). All interactions between main effects and group were nonsignificant, indicating both groups show the same pattern of basic effects (all ps > .30; see table 1).

We compared accuracies and reaction times between groups. Independent sample t-tests showed that multi-problem young adults were less accurate ($t = 2.33$, $p < .05$), but the groups did not significantly differ in reaction time ($p > .10$). See table 1 for an overview.

EEG results

First, the 2x2 mixed ANOVA with mean amplitude during 25-100 ms time window

Table 2. Correlation matrix of covariates, brain and behavioral measures of error processing, and psychopathic traits within the multi-problem sample (N=115)

	Age	IQ	ΔERN	Pe	Accuracy	Congruency effect	Correctness effect	PES	YPI Affective	YPI Interpersonal	YPI Behavioral	YPI Total
Age	1	-	-	-	-	-	-	-	-	-	-	-
IQ	-.015	1	-	-	-	-	-	-	-	-	-	-
ΔERN	-.003	-.194*	1	-	-	-	-	-	-	-	-	-
Pe	-.016	.153	-.096	1	-	-	-	-	-	-	-	-
Accuracy	-.028	.320**	-.568**	.082	1	-	-	-	-	-	-	-
Congruency effect	.231*	-.165	.091	-.085	-.227*	1	-	-	-	-	-	-
Correctness effect	-.079	.206*	-.110	.122	.150	-.140	1	-	-	-	-	-
PES	.040	.315**	-.348**	.008	.555**	-.121	.486**	1	-	-	-	-
YPI Interpersonal	-.044	.091	-.071	.156	.049	-.103	.046	-.016	1	-	-	-
YPI Affective	-.118	.074	-.052	.080	-.056	-.040	-.048	-.084	.391**	1	-	-
YPI Behavioral	-.168	.082	-.031	-.017	-.023	-.023	-.049	-.061	.420**	.367**	1	-
YPI Total	-.137	.107	-.068	.102	-.010	-.075	-.018	-.067	.805**	.761**	.745**	1

Note. IQ = Intelligence Quotient, ΔERN = Error-related negativity difference wave, Pe = error positivity, PES = post-error slowing, YPI = Youth Psychopathy Inventory, * = $p < .05$, ** = $p < .01$

as dependent variable revealed, as expected, a significant main effect of response condition (F = 143.71, p <.001), with incorrect responses showing larger negative amplitudes (M = -4.60 μV, SD = 4.54) than correct responses (M = 0.82 μV, SD = 3.46). Furthermore, there was a significant interaction with group (F =6.30, p < .05), with the differences in amplitude between incorrect and correct trials being larger in the control group (M = -7.55 μV, SD = 5.02) than in the multi-problem group (M = -4.94 μV, SD = 4.75). The 2x2 mixed ANOVA with mean amplitude during 250-400 ms time window as dependent variable also revealed a significant effect of response condition (F = 145.68, p < .001), with incorrect responses having larger amplitudes than correct responses, but showed no interaction with group (F = 1.91, p = .17). See table 1 for an overview, figure 1 for the EEG waveforms, and figure 2 for topographic information.

Second, within the multi-problem group, we performed correlation analyses between age, IQ, ΔERN, Pe, basic task effects, and psychopathy measures. We found significant correlations between age and the congruency effect (r = .231, p < .05), IQ and ΔERN (r = -.194, p < .05), IQ and accuracy (r = .320, p < .01), IQ and the correctness effect (r = .206, p <. 05), IQ and PES (r = .315, p <.01), ΔERN and PES (r = -.348, p < .01), and the correctness effect and PES (r = .486, p < .01), but no

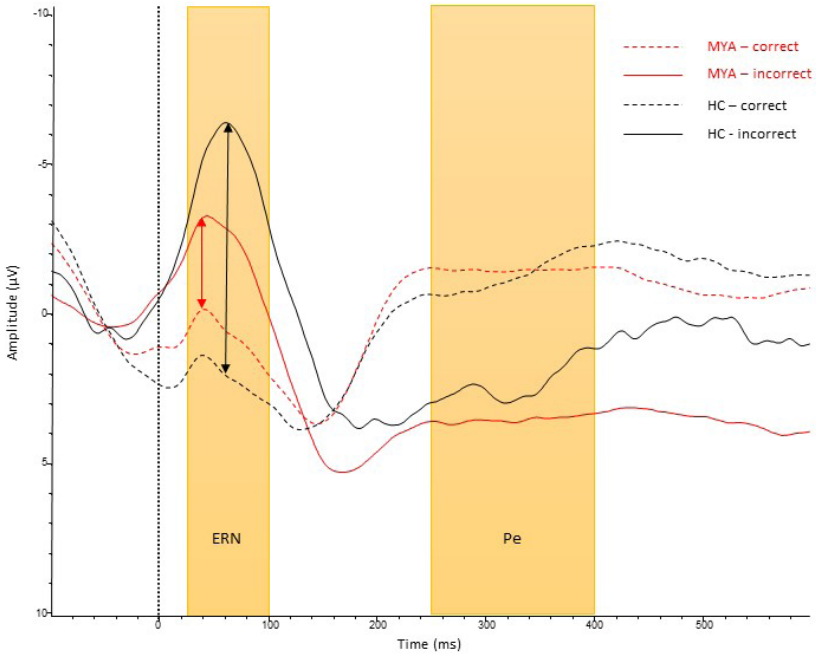

Figure 1. EEG waveforms to correct and incorrect trials for multi-problem young adults (MYA) and healthy controls (HC)

Table 3. Regression models within multi-problem young adults (N = 115)

Outcome	Predictor	ß	p-value ß	R^2	p-value R^2
ΔERN	Step 1: age	-0.005	.961	.043	.094
	Step 1: IQ	-0.208	.037		
	Step 2: age	-0.004	.968	.047	.408
	Step 2: IQ	-0.204	.037		
	Step 2: affective	-0.027	.799		
	Step 2: behavioral	0.035	.754		
	Step 2: interpersonal	-0.054	.629		
ΔERN	Step 1: age	-0.005	.961	.043	.094
	Step 1: IQ	-0.208	.037		
	Step 2: age	-0.010	.920	.045	.182
	Step 2: IQ	-0.204	.035		
	Step 2: total psychopathy	-0.039	.688		
Pe	Step 1: age	0.019	.846	.017	.404
	Step 1: IQ	0.128	.184		
	Step 2: age	0.009	.924	.050	.365
	Step 2: IQ	0.119	.220		
	Step 2: affective	0.048	.657		
	Step 2: behavioral	-0.128	.250		
	Step 2: interpersonal	0.181	.105		
Pe	Step 1: age	0.019	.846	.017	.404
	Step 1: IQ	0.128	.184		
	Step 2: age	0.030	.757	.025	.450
	Step 2: IQ	0.119	.221		
	Step 2: total psychopathy	0.089	.362		

significant correlations between the psychopathy and brain measures. See table 2 for an overview.

Third, we performed two hierarchical multiple linear regression analyses with the ERN difference wave as dependent variable, age and IQ as covariates entered in step 1, and either the three psychopathy subscales or the total psychopathy score as independent variables in step 2. In step 1, the model failed to reach significance ($F = 2.42$, $p = .09$, $R2 = .04$), although IQ was a significant predictor ($t = -2.20$, $p < .05$, $ß = -0.21$). In step 2, the addition of the three psychopathy subscales or the total psychopathy score did not significantly change the model and no psychopathy measures significantly predicted the ΔERN (all ps > .10). The addition of drug use as a covariate had no effect on the models. See table 3 for an overview.

Fourth, we performed two similar hierarchical multiple linear regression analyses, but with the Pe as dependent variable. In step 1, the model failed to reach significance ($F = 0.914$, $p = .40$, $R2 = .02$). In step 2, the addition of the three psychopathy subscales or the total psychopathy scores did not significantly change the model and no psychopathy measures significantly predicted the Pe (all ps > .10). The addition of drug use as a covariate had no effect on the models. See table 3 for an overview.

Discussion

In this study, we investigated the relationship between psychopathic traits and behavioral and neural indices of error processing in a large sample of multi-problem young adults and a healthy control group. Behaviorally, multi-problem young adults performed worse than controls, having lower accuracy rates. On a neural level, multi-problem young adults showed impaired early error-processing as indicated by a decreased ERN, but showed intact late error-processing as they had a similar Pe as the control group. Within the multi-problem group, neither total psychopathy scores nor psychopathic trait subscales were significantly related to any of the behavioral or brain measures. We did find associations between IQ and both behavioral and brain measures, in which a higher IQ always significantly related to better performance or

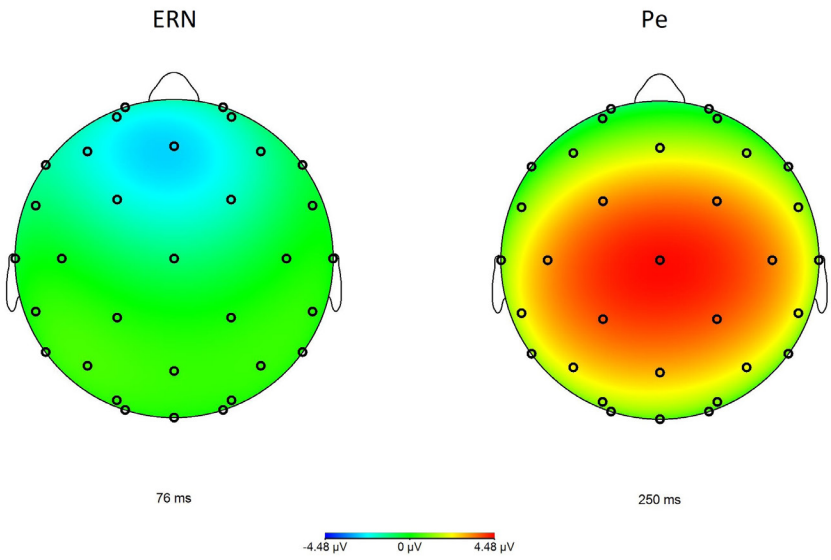

Figure 2. Topographic information for error-related negativity (ERN) and error positivity (Pe)

a greater effect: a larger ΔERN, higher accuracy, a larger effect of correctness, and greater post-error slowing.

Because multi-problem young adults suffer from a score of problems and form a heterogeneous sample, it is hard to assess which issues specifically caused them to perform worse on the Flanker task and show a decreased ERN compared to healthy controls. One factor that is likely to contribute is IQ, as our multi-problem sample has a low mean IQ of 82 and our results indicate that within this sample IQ is related to both behavioral and brain measures of error-processing. Although we did not assess IQ in our control group, we can assume their mean IQ to be in the average range as we selected them to have an average education. Another factor that probably contributes is externalizing behavior, which is likely to be more prevalent in our sample than in the general population, and previous research has shown externalizing behavior to be related to a decreased ERN (Hall, Bernat, & Patrick, 2007). Nonetheless, as within multi-problem young adults a large amount of individual variability in cognitive functioning and problem behavior may be present, it is difficult to properly assess the likelihood of these options. Thus, given the heterogeneity of problems that multi-problem young adults present with, we should be careful drawing strong conclusions concerning the nature of the differences in behavioral and neural performance between multi-problem young adults and healthy controls. One viable route of investigation may be to use statistical methods such as cluster analysis to assess whether subgroups with different (risk) profiles can be identified, and whether such groups differ in terms of error-related brain activity.

Our IQ findings suggest that participants with a higher IQ alter their behavior in response to errors to a greater degree than those with a lower IQ. Additionally, on the brain level they showed better automatic error-processing. Most studies investigating the relationship between psychopathy and error processing either did not measure IQ or they matched groups on IQ, but did not include IQ in further analyses. Notable exceptions are studies in incarcerated adolescents (Maurer et al., 2015) and incarcerated females (Maurer et al., 2016) where no association between ERN activity and IQ were found, and a study in incarcerated males (Steele et al., 2015) in which IQ was positively related to ERN activity. Although specific results are slim, our findings complement the view of Blair (2013) that IQ is of relevance to brain studies in psychopathy and thus should at least be matched on or controlled for. Furthermore, our study suggests that IQ may be especially relevant to consider in samples with low intelligence. Possibly, IQ differences in the lower range have a larger impact on error processing than those in normal and higher ranges.

In line with previous research, within our sample of multi-problem young adults we found no significant association between psychopathic traits and the ERN in an affectively neutral task, adding to the evidence that early error processing is intact in psychopathy. Likewise, we found no significant relationship between

psychopathic traits and behavioral measures of error-processing. Unexpectedly, we also did not find a significant relationship between psychopathic traits and the Pe. An interesting explanation for this finding may be that with age the relationship between psychopathic traits and the Pe changes. Maurer and colleagues (2015) have suggested that it may be the case that adolescents with elevated psychopathic traits suffer from late error processing deficits (i.e., a negative relationship between psychopathic traits and the Pe), but that the relationship reverses in adulthood as a compensatory mechanism. In this manner, the brain attempts to overcome the initial error processing deficits present in adolescence. This could explain why in adolescents (mean age 17) a negative relationship between psychopathic traits and Pe has been found (Maurer et al., 2015), but in adults (mean age 34) a positive relationship between psychopathic traits and Pe has been found (Steele et al., 2015). If so, it could be speculated our sample of young adults (mean age 22) may not only be in a developmental transition period distinct from adolescence, but also in a transitional period between error-processing deficits and error-processing overcompensation. Thus, this null finding may be due to the specific age range of our sample. Additionally, it is possible that the Pe changes with age in general. Meta-analytic research has shown that another often investigated ERP, the P300, does indeed change with age (van Dinteren, Arns, Jongsma, & Kessels, 2014), but for the Pe such large-scale analyses have, to our knowledge, not been performed. Some studies have not found evidence for a change in Pe from childhood to young adulthood (Davies, Segalowitz, & Gavin, 2004; Santesso, Segalowitz, & Schmidt, 2006), but others have found a Pe increase over time in children (Grammer, Carrasco, Gehring, & Morrison, 2014). Within our own sample, the age range of participants was likely too small to uncover such effects and longitudinal research is warranted to establish the change of the Pe with age.

Another explanation could lie in the fact that in the current study we employed a self-report measure of psychopathy. One recent study found differential relations between error-related brain activity and different measures of psychopathy in the same sample (Maurer et al., 2018). Specifically, this study found an association between the Pe and Facet 4 of the Psychopathy Checklist Youth Version (PCL:YV; Hare, 2003), but not between the Pe and four different self-report measures of psychopathy, including the YPI. It is possible that error-related brain dysfunction is specifically related to features not captured by the self-report measures. Of course, a final possibility is that there is no true relation between psychopathic traits and the Pe. Older studies (Brazil et al., 2009; Munro et al., 2007) into this relationship have been performed in small samples and had a dichotomic approach (no more than 16 participants in the psychopathic groups, no more than 18 participants in the control groups before exclusion). More recent, well-powered, and dimensional studies (Maurer et al., 2015; Maurer et al., 2016; Steele et al., 2015) have found only small effect sizes and the direction of the effect has been inconsistent. However, evidence

for cognitive deficits in psychopathy is abundant (Blair, 2013; Kiehl, 2006), suggesting it is unlikely that on a neural level they perform as normal. Therefore, it would be informative for future research to 1) perform studies in large samples which take into account the general effects of age on the Pe, for example by including larger age ranges (e.g., 16 to 35 years); 2) ensure that the entire range of psychopathic traits is captured in these samples; and 3) investigate the development of the relationship between psychopathic traits and the Pe by performing follow-up measurements in the same samples and test for an interaction effect between psychopathic traits and age change. If the theory of overcompensation holds, it should be shown that this effect is specific to psychopathic traits and not a general mechanism that occurs in people with a small Pe.

Limitations in the comparability of our study to others lie in the fact that we used a self-report measure to assess psychopathic traits, rather than the more extensive PCL-YV (Hare, 2003). Although the YPI has good validity (Colins & Andershed, 2015) and correlates with the PCL-YV (Andershed et al., 2007) it has also been suggested that the subscales of these measures are not interchangeable (Fink et al., 2012) and this should be taken into account when interpreting the data. Another noteworthy difference between our study and others is that our sample has a low average IQ (mean = 82), whereas other samples of which the IQ is reported have mean IQs in the normal range. Although this limits the generalizability to samples with higher IQs, below average IQs are common in forensic populations and may be relevant to study distinctly, especially since we found IQ to be related to both behavioral and brain measures of error processing. Finally, we have not specifically sampled for high psychopathic traits, but rather included a sample which we know to present with antisocial behavior. Possibly, our disparate Pe results compared to other studies may be due to multi-problem young adults presenting with more externalizing, but not specifically psychopathic problems.

In conclusion, we found evidence for dysfunctional error-processing on both behavioral and early neural indices in a group of multi-problem young adults, but did not find evidence for a relationship between psychopathic traits and dysfunctional error-processing. Future research may elucidate whether this is due to our young adult participants being in a transitional period in between error-processing deficits and error-processing overcompensation.

Chapter 5: No association between antisocial behavior and autonomic functioning in multi-problem young adults

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In submission

Abstract

Aberrant functioning of the autonomic nervous system (ANS) seems to be an important neurobiological factor in the occurrence of antisocial behavior. Both baseline autonomic functioning and the responsivity of the ANS have been related to various types of antisocial behavior, including psychopathic traits and aggression. Here we investigated whether a naturalistic sample of male multi-problem young adults (age 18-27) present with similar autonomic deficits in relation to their antisocial behavior as previous studies observed in clinical samples. In a final sample of 112 multi-problem young adults, baseline autonomic functioning and autonomic responsivity to emotional stimuli were assessed through four physiological measures: heart rate, respiratory sinus arrhythmia, pre-ejection period, and skin conductance level. 27 control participants were included primarily to assess whether the task worked appropriately. Participants watched a 5-minute video without emotional content to assess baseline autonomic functioning and watched two short clips in which sad events took place to assess autonomic changes in reaction to sadness. We investigated the relationship between autonomic functioning and self-reported antisocial behavior (i.e. psychopathic traits and aggression) within the multi-problem group. We found no relationship between antisocial behavior and autonomic functioning on baseline nor on responsivity measures. These null-findings highlight the importance of research in naturalistic samples in addition to research in clinical and general populations samples and underscore the complexity of translating research findings into practical and clinical implications.

Introduction

The autonomic nervous system (ANS) has long been implicated to play an important role in the occurrence of antisocial behavior. It consists of two branches that counteract each other, which combined activities should result in maintaining homeostasis. The sympathetic nervous system (SNS) activates the body in response to stressors and can be measured through heart rate (HR), the pre-ejection period (PEP; time between onset of ventricular depolarization and opening of the aortic valves), and skin conductance level (SCL; van Lien, Schutte, Meijer, & de Geus, 2013). The parasympathetic nervous system (PNS) has an inhibitory function on the SNS and thus (re)turns the body to rest. The PNS can be measured through HR and respiratory sinus arrhythmia (RSA; the variability in heart rate between expiration and inspiration; Grossman & Taylor, 2007). Note that as HR is influenced by both the SNS (HR increase) and PNS (HR decrease) it is not a pure marker of either two. Historically, two dominant theories exist concerning the relationship between ANS activity and reactivity, and antisocial behavior. Low arousal theory proposes that individuals with a hypoactive ANS attempt to elevate their arousal to a preferred level by displaying antisocial behavior. Alternatively, fearlessness theory posits that low arousal is indicative of a lack of fear for negative consequences of actions, resulting in increased engagement in antisocial behavior (Raine, 1993). Both theories predict that resting ANS activity is attenuated in antisocial behavior.

For decades, research has been performed on resting HR, which is the most thoroughly investigated biological correlate of antisocial behavior. Low resting HR has been meta-analytically shown to be related to various antisocial disorders and behaviors including conduct disorder/oppositional defiant disorder (CD/ODD), offending, aggression, and psychopathy (Lorber, 2004; Ortiz & Raine, 2004; Portnoy & Farrington, 2015). However, effect sizes of the relationship have been shrinking with time (Portnoy & Farrington, 2015) and some recent, large-scale studies have failed to find significant associations (Oldenhof et al., 2018; Prätzlich et al., 2018). The relationship between other resting measures of the ANS and antisocial behavior has not been investigated as intensively as HR, but studies suggest that increased resting PEP is related to conduct problems and aggression (Beauchaine et al., 2013); reduced resting SCL is related to psychopathy and conduct problems (Lorber, 2004); and reduced resting RSA is related to externalizing problems and antisocial behavior (Beauchaine, Gatzke-Kopp, & Mead, 2007; De Wied, Boxtel, Posthumus, Goudena, & Matthys, 2009; Graziano & Derefinko, 2013).

Similarly, diminished reactivity of the ANS to stressors (e.g., movies to elicit emotional reaction or loud noises to elicit a startle response) has been found to be related to antisocial behavior. A meta-analysis showed that HR reactivity during stressors is related to antisocial behavior (Ortiz & Raine, 2004); less PEP reactivity has

been observed in conduct disorder (Beauchaine et al., 2007); reduced SCL reactivity has been found to be related to conduct problems and aggression (Herpertz et al., 2001); and reduced RSA reactivity has been demonstrated in conduct problems (Marsh, Beauchaine, & Williams, 2008). Specifically, autonomic reactivity to negative emotions seems to be affected (Beauchaine et al., 2019). In sum, there is evidence for associations between antisocial behavior and both resting and reactivity measures of the ANS. However, some null-results and discordant findings are present in the literature (e.g., de Wied et al., 2009; Zahn & Kruesi, 1993) and it is unclear whether results hold up across types of antisocial behavior, age ranges, and populations.

As for differences in populations, the greatest focus in research on the relationship between antisocial behavior and autonomic functioning has been on children with CD and ODD, or adolescents with psychopathic traits and aggressive problems. There is a need to further research this relationship in adult samples to (dis) confirm the hypothesis that aberrant autonomic functioning is related to antisocial behavior across the life-course. Thus far, especially little emphasis has been given to the specific period of young adulthood, even though it is now regarded as a distinct developmental stage in which both psychosocial and neurobiological changes occur (Arnett, 2000). Vulnerable populations transitioning into adulthood may be especially relevant to study (Osgood et al., 2010) as they are at an increased risk to persevere in their antisocial behavior or even develop it further (Hill, Blokland, & Van Der Geest, 2018). Multi-problem young adults (18-27) are such a vulnerable population: they lack a stable income, do not have the prerequisites to get a job, have problems in multiple life domains, and 66% have had Child Protection Service (CPS) interference, chiefly due to judicial problems before age 18 (van Duin et al., 2017). As they form a naturalistic sample with heterogeneous problems, we can expect their psychopathic traits and aggressive behavior to vary accordingly. This allows for a dimensional approach that includes the full range of antisocial behavior and optimizes power.

Thus, in the current study we sought to investigate in a naturalistic sample of multi-problem young adults whether (1) resting measures of the ANS are related to psychopathic traits and aggression, and whether (2) ANS reactivity to emotional stimuli is related to psychopathic traits and aggression. We included a group of healthy controls primarily to assess whether the task worked appropriately and to exploratively investigate whether multi-problem young adults as a group perform differently compared to a healthy population. We expected to find lower resting levels of the ANS, as well as lower reactivity of the ANS, to be related to both psychopathic traits and aggression.

Method

Participants

Participants were 127 male multi-problem young adults (part of a larger study; Luijks et al., 2017). Multi-problem young adults are characterized by a lack of income and education, as well as problems in multiple life domains such as addiction, mental health problems, and judicial problems. In our sample, 83% has a criminal record and self-reported delinquency ranges from 10-30% in the last six months and from 61-86% during lifetime, depending on the type of offence (see table 1). Participants were recruited at the start of day treatment program De Nieuwe Kans (DNK; translated as "New Opportunities"). DNK provides a multimodal approach, which aims to increase self-sufficiency and ultimately decrease negative outcomes such as recidivism of multi-problem young adults. This program employs cognitive behavioral techniques and rehabilitation components, such as cognitive skills training, drug treatment, and education.

Additionally, 27 age and gender group matched healthy controls were included in the study. Controls were selected to have average education. Of the multi-problem young adults, 4 were excluded because they failed to complete the task and 11 were excluded because of technical errors with the measuring equipment. Additionally, 5 control subjects were excluded because of technical errors with the measuring equipment. Thus, the final sample included 112 multi-problem young adults and 22 healthy controls.

All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. The study has been approved by the Medical Ethical Committee of the VU University Medical Center (registration number 2013.422 - NL46906.029.13) and all participants provided written informed consent. In addition to the ANS protocol, an fMRI protocol was administered on another day. Participants received a reimbursement of 30 euros total for their participation in both of the sessions.

Instruments

As a measure of psychopathic traits, we employed the Youth Psychopathy Inventory – Short Version (van Baardewijk et al., 2010). The YPI-SV is a self-report measure that distinguishes three factors of psychopathy: an affective callous-unemotional factor, a behavioral impulsive-irresponsible factor, and an interpersonal grandiose-manipulative factor. It has been validated in young adults (Colins & Andershed, 2015).

Table 1. Questionnaire and autonomic baseline measures

	Multi-problem young adults (N = 112)		Healthy controls (N = 22)		
	M	SD	M	SD	p
Age (years)	22.42	2.38	22.51	2.45	.877
IQ	82.64	10.35	.	.	.
Education					
No secondary education	93%	.	0%	.	.
Secondary education following	0%	.	42%	.	.
Secondary education finished	7%	.	58%	.	.
Psychopathy					
YPI interpersonal	11.39	3.96	13.14	3.50	.061
YPI affective	10.65	3.44	11.76	3.27	.176
YPI behavioral	12.27	3.27	12.33	3.07	.938
YPI total	34.32	8.12	37.24	6.46	.122
Aggression					
RPQ Reactive aggression	11.39	4.57	9.23	5.34	.050
RPQ Proactive aggression	5.44	4.42	4.14	4.54	.211
RPQ Total	16.83	7.88	13.36	9.43	.070
Cannabis Use					
Cannabis use past 30 days	13.93	13.51	4.50	7.02	<.001
Years of regular cannabis use	4.18	3.73	1.30	2.72	<.001
Self-reported delinquency					
Destruction/public order offence – lifetime	71%	.	.	.	.
Property offence – lifetime	86%	.	.	.	.
Aggression/violent offence – lifetime	71%	.	.	.	.
Drug offence – lifetime	61%	.	.	.	.
Autonomic resting measures					
Heart rate (bpm)	65.32	9.21	66.81	9.48	.491
Respiratory sinus arrhythmia	94.47	42.40	89.50	41.12	.614
Pre-ejection period (ms)	111.85	16.64	111.74	25.70	.979
Skin conductance level (μS)	5.03	3.19	3.93	2.49	.129

As a measure of aggression, we employed the Reactive Proactive Questionnaire (Cima et al., 2013; Raine, Dodge, Loeber, Gatzke-kopp, Lynam, Reynolds, Stouthamer-Loeber, et al., 2006). The RPQ consists of two subscales: reactive aggression and proactive aggression. We used the Measurements in the Addictions for Triage and Evaluation Questionnaire (MATE) to assess current and historic cannabis use. In order to measure intelligence, we used the short form of the Wechsler Adult Intelligence Scale third version (WAIS-III SF) consisting of four subtests (Blyler et al., 2000): digit symbol coding, information, block design, and arithmetic. The WAIS-III-SF was only assessed in the multi-problem group.

Task & Procedure

Participants were first shown a 5-minute excerpt from the video Coral Sea Dreaming (Small World Music Inc.) to assess resting levels of the ANS. Previous research has shown that watching this video results in a better measurement of resting levels than sitting quietly (Piferi, Kline, Younger, & Lawler, 2000). Then, participants watched two sad film clips intended to evoke an empathic response to the emotion sadness. One clip involves a boy crying because he did not make the selection of a soccer team (Mohammed), the other clip portrays a boy crying over the loss of his father (Champ). Previous research has shown that both clips reliably evoke sadness in participants (de Wied et al., 2009; Gross & Levenson, 1995) respectively). Before each clip, a 1-minute excerpt of the Coral Seas Dreaming video was shown to be used as baseline. The clips were counterbalanced across participants. After each clip, participants indicated how they thought the boy in the clip by rating the emotions happiness, anger, fear, and sadness on a 5-point Likert scale.

Measurements were performed in the Erasmus Behavioral Lab of the Institute for Psychology at the Erasmus University Rotterdam. Participants were seated in a comfortable chair in a sound-attenuated room with dimmed lights. A trained researcher gave a standardized explanation to each participant concerning the entire protocol. Additionally, a short introduction appeared on the screen before each film clip, indicating when participants simply had to watch the clip (in the case of Coral Sea Dreaming) or also had to answer a few questions about it (in the case of Mohammed and Champ) concerning what emotion they thought the boys in the videos showed and what emotions they themselves experienced while watching the videos.

Physiological recording and processing

We used the VU Ambulatory Monitoring System (VU-AMS; Klaver, De Geus, & De Vries, 1994) to record both the electrocardiogram (ECG) and impedance cardiogram (ICG), as well as the level of skin conductance. Five electrodes were placed on the chest, two on the back, and two on the second phalanges of the non-dominant hand according to

the VU-AMS manual (http://www.vu-ams.nl/support/instruction-manual/).

Data processing was performed with the VU-AMS Data, Analysis & Management Software (VU-DAMS). Heart rate (HR) was assessed by automated counting of the R-peaks; respiratory sinus arrhythmia (RSA) was defined as the longest period between heart beats during expiration minus the shortest period between heart beats during inspiration; pre-ejection period (PEP) was defined as the time between the onset of left ventricular depolarization and opening of the aortic valve; skin conductance level (SCL) is presented in microSiemens.

Data analysis

In order to assess whether the task validly elicited sadness-related physiological reactions we performed paired-sample t-tests comparing physiological activity during baseline and film clips for each physiological measure (HR, RSA, PEP, SCL). We tested whether the responses differed between the clips by performing paired-sample t-tests.

For the questionnaire data and physiological data, we used independent sample t-tests with group as independent variable to compare the multi-problem group with the healthy control group. For the analysis of the behavioral responses, we used Mann-Whitney U tests to compare the groups. We used Pearson correlations to establish the relation between psychopathic traits and aggression and established variance inflation factors to assess whether multicollinearity would be an issue for further analyses. We used linear regression analyses to investigate the relation between psychopathic traits, aggression, and physiological measures within the multi-problem group.

Results

Task validity: physiological responses to sadness clips

Paired sample t-tests showed that there were significant autonomic changes in response to the sadness clips. HR decelerated in both Mohammed ($M = -1.61$, $t = -3.89$, $p < .001$) and Champ ($M = -2.63$, $t = -7.74$, $p < .001$); RSA lowered in both Mohammed ($M = -12.15$, $t = -2.86$, $p < .01$) and Champ ($M = -15.56$, $t = -5.35$, $p < .001$); SCL lowered in both Mohammed ($M = -0.43$, $t = -6.35$, $p < .001$) and Champ ($M = -0.27$, $t = -4.63$, $p < .001$). We found no significant changes in PEP (both $ps > .05$). Paired-sample t-tests between the difference scores for Mohammed and Champ indicated no significant differences between the autonomic responses to the clips, except for HR. The HR deceleration was larger for Champ than for Mohammed ($M = -0.99$, t -2.16, $p < .05$).

Table 2. Behavioral and autonomic responses to sadness

	Multi-problem young adults (N = 112)		Healthy controls (N = 22)		
	M	SD	M	SD	p
Behavioral response					
Happiness – Mohammed	1.32	0.93	1.00	0.00	.067
Happiness – Champ	1.37	1.11	1.00	0.00	.106
Anger – Mohammed	2.27	1.19	2.00	0.93	.414
Anger – Champ	2.26	1.35	2.09	1.19	.691
Fear – Mohammed	2.10	1.13	2.41	1.30	.709
Fear – Champ	3.32	1.33	3.45	1.14	.721
Sadness – Mohammed	4.60	0.84	4.77	0.43	.609
Sadness – Champ	4.88	0.35	5.00	0.00	.106
Autonomic response					
HR (bpm) – Mohammed	-1.46	4.97	-2.34	3.14	.426
HR (bpm) – Champ	-2.66	3.95	-2.50	3.69	.863
RSA – Mohammed	-14.22	47.12	-2.15	51.93	.322
RSA – Champ	-16.57	34.43	-10.60	26.89	.445
PEP (ms) – Mohammed	2.71	16.33	2.22	10.24	.896
PEP (ms) – Champ	0.87	13.89	0.18	10.42	.833
SCL (μS) – Mohammed	-0.45	0.82	-0.32	0.44	.298
SCL (μS) – Champ	-0.29	0.73	-0.17	0.29	.449

Correlations between psychopathic traits and aggression and variance inflations factors

Within the multi-problem group, we found significant correlations between most of the psychopathy and aggression subscales (see table 3 for an overview). Variance inflation factors indicated no issues of multicollinearity (all VIFs < 1.8)

Relation between ANS functioning and psychopathic traits and aggression in the multi-problem group

Within the multi-problem group, we performed four linear regression analyses with HR, RSA, PEP, and SCL as outcome measures. In each model, the psychopathy and aggression subscales were entered as predictors. None of these models were significant (all ps > .05; see table 4 for an overview).

Similarly, within the multi-problem group, we performed four linear regression analyses with HR, RSA, PEP, and SCL change as outcome measures. In each model, the psychopathy and aggression subscales were entered as predictors. None of these models were significant (all ps > .05; see table 5 for an overview).

Table 3. Correlations between measures of psychopathy and aggression (multi-problem group only)

	Proactive aggression	Reactive aggression	Total aggression	YPI Interpersonal	YPI Affective	YPI Behavioral	YPI Total
Proactive aggression	.	.	.	.	.	.	.
Reactive aggression	.539**	.	.	.	.	.	.
Total aggression	.882**	.873**	.	.	.	.	.
YPI Interpersonal	.217*	.359**	.324**	.	.	.	.
YPI Affective	.133	.199*	.187*	.356**	.	.	.
Ypi Behavioral	.474**	.461**	.528**	.433**	.301**	.	.
YPI Total	.353**	.445**	.451**	.813**	.719**	.741**	.

* Correlation is significant at the 0.05 level (2-tailed).

** Correlation is significant at the 0.01 level (2-tailed).

Explorative comparison between multi-problem young adults and controls

Multi-problem young adults did not differ from controls on any of the psychopathy and aggression scales (all other ps > .05), with the exception of the Reactive aggression scale (p = .05) on which multi-problem young adults have higher scores than controls. Multi-problem young adults use more cannabis and have a longer history of regular cannabis use than controls (both ps < .001). The average IQ in the multi-problem group was 82.64 (see table 1 for an overview).

We found no significant differences between the multi-problem group and the control group on the four physiological measurements of the ANS during the 5-minute baseline video (all ps > .05; see table 1 for an overview).

Multi-problem young adults did not differ from the control group in their assessments of the emotion of the boys depicted in the film clips (for both clips and all emotions all ps > .05; see table 2 for an overview). The multi-problem young adults and controls did not differ in their autonomic reactions to the film clips (all ps > .05; see table 2 for an overview of the difference scores for each group).

Table 4. ANS baseline regression models within multi-problem young adults (N = 112)

Outcome	Predictor	β	p-value β	R^2	p-value R^2
HR	Interpersonal	-0.035	.751	.073	.155
	Affective	-0.011	.913		
	Behavioral	0.243	.044		
	Reactive aggressive	-0.015	.899		
	Proactive aggressive	-0.268	.029		
RSA	Interpersonal	0.117	.298	.055	.307
	Affective	-0.163	.118		
	Behavioral	-0.142	.241		
	Reactive aggressive	0.178	.144		
	Proactive aggressive	-0.004	.973		
PEP	Interpersonal	0.011	.921	.063	.237
	Affective	-0.131	.211		
	Behavioral	-0.160	.189		
	Reactive aggressive	0.232	.059		
	Proactive aggressive	-0.071	.565		
SCL	Interpersonal	0.040	.722	.066	.204
	Affective	0.006	.950		
	Behavioral	0.225	.063		
	Reactive aggressive	0.100	.410		
	Proactive aggressive	-0.230	.062		

Discussion

In this study we investigated the relationship between psychopathic traits, aggression, and both the physiological activity and responsivity of the ANS in a large, naturalistic sample of multi-problem young adults. We studied four measures of the ANS (heart rate, respiratory sinus arrhythmia, pre-ejection period, and skin conductance) to capture both SNS and PNS activity. We adopted a dimensional approach as to include the full range of antisocial behavior and optimize power.

Contrary to our expectations, within the multi-problem group we found no associations between any of the psychophysiological measurements and their psychopathic traits and aggressive behavior. This is at odds with previous studies e.g. (Latvala et al., 2015; Murray et al., 2016), although other recent studies also failed to find significant associations (Oldenhof et al., 2018; Prätzlich et al., 2018). Additionally, specifically the relationship between low resting heart rate and antisocial behavior has been weakening over the years of research (Portnoy & Farrington, 2015). This may

Table 5. ANS reactivity regression models within multi-problem young adults (N = 112)

Outcome	Predictor	β	p-value β	R^2	p-value R^2
HR	Interpersonal	0.163	.162	.050	.394
	Affective	0.098	.368		
	Behavioral	-0.062	.612		
	Reactive aggressive	0.040	.742		
	Proactive aggressive	-0.212	.089		
RSA	Interpersonal	0.101	.387	.059	.303
	Affective	0.143	.189		
	Behavioral	0.010	.937		
	Reactive aggressive	-0.094	.443		
	Proactive aggressive	-0.175	.163		
PEP	Interpersonal	-0.071	.540	.075	.170
	Affective	-0.025	.817		
	Behavioral	0.017	.887		
	Reactive aggressive	-0.009	.939		
	Proactive aggressive	-0.232	.061		
SCL	Interpersonal	-0.086	.451	.057	.301
	Affective	0.119	.268		
	Behavioral	-0.177	.146		
	Reactive aggressive	-0.114	.348		
	Proactive aggressive	0.169	.169		

be explained by the "proteus phenomenon", which entails the effect that in the early phase of investigation, both positive and negative significant findings are published. Later, findings refuting the original results become more attractive and null-findings are published more often. Our null-findings cannot be attributed to problems with the experiment, as autonomic changes from baseline measurements to film clip measurements were present in the right direction (Kreibig, 2010) and clearly visible in both multi-problem young adults and controls, indicating that the task worked appropriately and our autonomic measures are valid. Possibly, the relationship between ANS and antisocial behavior is stronger in childhood and adolescence and diminishes into adulthood. For baseline findings this is a realistic possibility, as meta-analytic effect sizes for adults have shown to be about twice as small as effect sizes in children and adolescents (Portnoy & Farrington, 2015). Another possibility is that because due to its naturalistic nature our sample is necessarily heterogeneous, which could account for diminished effect sizes. This is important as when we try to translate research findings into practical and clinical implications we unavoidably move from more controlled and selected populations and environments to more natural populations and environments. Of course, another explanation for these null-findings is that simply no relation between antisocial behavior and ANS (re)activity exists in multi-problem young adults. Finally, we cannot exclude the possibility that autonomic functioning may be hampered specifically in subgroups of individuals with more extreme levels of antisocial behavior, which may be underrepresented in our sample. Although multi-problem young adults present with clear antisocial behavior, they show robust and normative autonomic responses to sadness as measured with HR, RSA, and SCL.

In explorative analyses, we found no differences between multi-problem young adults and controls on both baseline and responsivity measures of the ANS. These findings are somewhat harder to interpret as multi-problem young adults suffer from a plethora of antisocial problems, but our sample does not differ from controls in terms of psychopathic traits and only slightly on aggression. Given the forensic nature of our sample it seems unexpected that multi-problem young adults would have similar psychopathy scores to healthy controls. However, more studies have found this to be the case in forensic samples (e.g. Aghajani et al., 2017; Boonmann et al., 2015). It may be representative of the fact that the YPI, contrary to for example the Psychopathy Checklist Youth Version, does not include criminal behavior per se in its definition of psychopathy. Additionally, as our healthy control group scores fairly high on measures of aggression compared to other non-offender groups (see Cima et al., 2013) and psychopathy and aggression are positively related, it may be coincidental that we have recruited a control group scoring relatively high on both psychopathy and aggression.

This study is limited by the use of a fairly small control group, because its

main purpose was to assess task validity. This provides limited interpretability of the analyses comparing participants and controls, although other studies have used experimental groups of similar size (e.g. de Wied et al., 2009; de Wied, van Boxtel, Matthys, & Meeus, 2012). In contrast, our study is strengthened by its large sample size in terms of autonomic responsivity. Whereas studies investigating baseline autonomic activity are more often large and well-powered (e.g. Latvala et al., 2015; Prätzlich et al., 2018), studies looking into autonomic responsivity commonly have group designs with group sizes of 15 to 35 participants (e.g. Beauchaine et al., 2007; de Wied et al., 2012; Marsh et al., 2008), limiting the generalizability of results.

In conclusion, in a large, naturalistic sample of multi-problem young adults we found no evidence for a relationship between resting ANS functioning and antisocial behavior, nor did we find evidence for a relationship between ANS reactivity and antisocial behavior. Our null-findings highlight the need for research with more naturalistic samples, as results may be at odds with findings from clinical samples.

Chapter 6: The predictive value of neurobiological measures for recidivism in delinquent young adults

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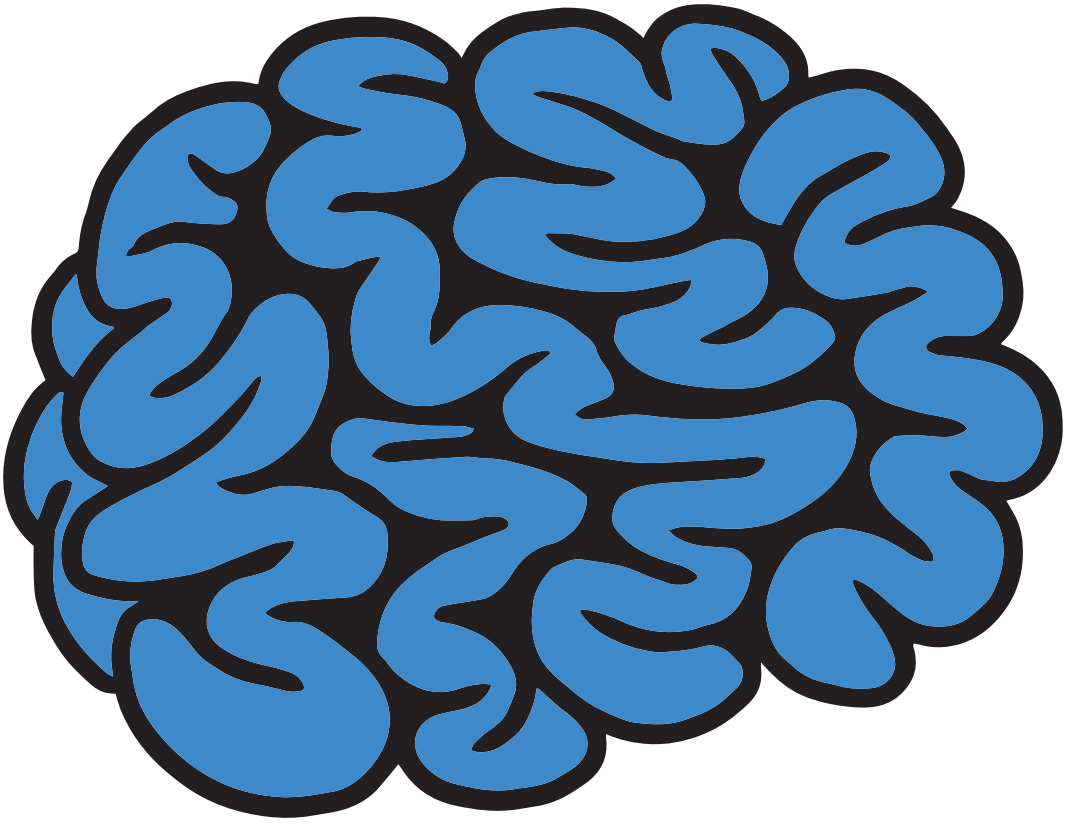
In submission



Abstract

Neurobiological measures have been associated with delinquent behavior, but little is known about the predictive power of these measures for criminal recidivism and whether they have incremental value over and above demographic and behavioral measures. This study examined whether selected measures of autonomic functioning, functional neuroimaging, and electroencephalography predict overall and serious recidivism in a sample of 127 delinquent young adults. We assessed demographics and intelligence; previous delinquency and drug use; behavioral traits including aggression and psychopathy; and neurobiological measures including heart rate, heart rate variability, functional brain activity during an inhibition task, and two electroencephalographic measures of error processing. We tested longitudinal associations with recidivism using Cox proportional hazard models and predictive power using C-indexes. Past offenses, long-term cannabis use, and reactive aggression were strongly associated with recidivism, as were the neurobiological measures resting heart rate and error processing. In the predictive model, demographics, past delinquency, drug use, and behavioral traits had moderate predictive power for overall and serious recidivism (C-index over 30 months [C30] = 0.68 and C30 = 0.75, respectively). Adding neurobiological measures to the predictive model significantly improved predictive power (C30 = 0.72 and C30 = 0.80, respectively). This study shows that demographic and behavioral characteristics longitudinally predict recidivism in delinquent young adults, and that the addition of neurobiological measures improves the model. This results in a good predictive function, particularly for serious recidivism. Importantly, the most feasible measures, autonomic functioning and electroencephalography, prove to be useful predictors.

Introduction

Delinquent behavior is a major psychiatric and public safety issue with severe consequences for both individuals and society (McCollister et al., 2011). Several longitudinal studies have advanced our etiological understanding of delinquent behavior and helped to identify various relevant risk-factors for these behaviors, including age, sex, criminal history, drug use, and behavioral problems (Cottle, Lee, & Heilbrun, 2001). Despite advances in the knowledge on the involvement of neurobiological mechanisms in the etiology of delinquency, there are only a few studies integrating neurobiological measures in longitudinal prediction studies.

One of these advances is our knowledge on the relation between the autonomic nervous system and delinquency. Resting heart rate (HR) is arguably the best-replicated physiological correlate of antisocial behavior (Lorber, 2004b; Ortiz & Raine, 2004). Several decades ago, Wadsworth et al. (1976) demonstrated that lower childhood heart rate predicted delinquency. Similarly, Raine and colleagues (Raine et al., 1997) related lower heart rate to antisocial behavior in general population and high-risk samples. A seminal study in Swedish conscripts provided strong evidence that HR at age 18 is longitudinally related to violent and nonviolent delinquency (Latvala et al., 2015). Heart rate variability (HRV), as measured by respiratory sinus arrhythmia (RSA), is a related neurobiological measure associated with antisocial behavior, albeit less consistently (e.g. Beauchaine, Hong, & Marsh, 2008; Dietrich et al., 2007). More recently, functional imaging research has been used in cross-sectional studies to compare brain activity between antisocial cases and controls. These studies show that prefrontal brain functioning seems to be impaired in antisocial behavior, specifically in the orbitofrontal, dorsolateral frontal, and anterior cingulate cortex (ACC; see Yang & Raine, 2009). Finally, a series of electrophysiological studies compared evoked potential in studies of delinquent populations, and found aberrant brain responses to errors in delinquents (Brazil et al., 2009; Steele, Maurer, et al., 2015). It is, however, unclear whether these neurobiological variables independently predict delinquency. This knowledge is important to optimize risk assessment and to tailor treatment for at risk populations.

Although some studies have associated neurobiological measures with delinquent behavior, only few studies have employed such measures in formal prediction models to make adequate and reliable prognoses. In the last years, a few epidemiological studies assessed the validity and utility of prediction models for delinquent behavior using a formal approach. Aharoni et al. (2013) employed functional magnetic resonance imaging (fMRI) in criminal offenders (N=96) to investigate whether a neurobiological measure of inhibition (i.e. functional brain activity during a Go-Nogo task) added to the prediction of recidivism. They found decreased activity in the anterior cingulate cortex (ACC) to be predictive of rearrest. Thus far, the only

study to include several neurobiological measures has been performed in a small subsample (N=45) of the same cohort, in which two electroencephalographical (EEG) measures of error processing were also investigated. The error-related negativity (ERN), a measure of early error processing was not predictive of rearrest, but a greater error positivity (Pe), a measure of late error processing did predict rearrest (Steele, Claus, et al., 2015). When the EEG and fMRI measures were included in the same model ACC activity did not predict rearrest anymore, possibly because the various factors measure the same process. Since well-powered studies of the joint and individual contribution of several neurobiological parameters tested simultaneously are lacking, to date it is still unknown whether different neurobiological parameters independently predict delinquency. This paper aims to address this gap in knowledge.

This study was conducted in a large sample of young adults who were followed up to four years for the incidence of delinquency. An extensive battery of demographic and self-report measures including age, ethnicity, education, intelligence, internalizing and externalizing psychopathology, and aggressive and psychopathic behavior was assessed and its predictive power evaluated. This is important, as assessment of these variables is feasible in most instances and practitioners would certainly not include any costly neurobiological measures in prediction models if they did not outperform interview or questionnaire measures. We included five neurobiological measures: baseline autonomic functioning (HR and RSA), electroencephalographic measures of error processing (ERN and Pe), and fMRI activity of the ACC during response inhibition. The first aim of this study was to test the prospective association of demographic and behavioral measures, and neurobiological measures with criminal recidivism. The second aim was to formally test the predictive power of different domains of variables. The main goal was to examine which neurobiological parameters meaningfully add to the prediction of overall and serious recidivism over and above demographic and behavioral measures.

Methods and Materials

Participants

Participants were 127 male young adults aged 18-27 (mean age 21.92, SD 2.40) recruited when they started a day treatment program at De Nieuwe Kans (DNK; translated as “New Opportunities”) in Rotterdam, The Netherlands. DNK provides a multimodal day treatment program for “multi-problem” young adults with a history of delinquency (81% had a criminal record), low or no income, poor job skills, and drug use (53% has regularly used cannabis for at least 5 years). This program employs cognitive behavioral techniques and rehabilitation components, such as cognitive

skills training, drug treatment, and education (see Luijks et al., 2017). This study is part of a larger cohort study which includes 696 young adults, followed for a period of 14 months and interviewed at four separate occasions (Luijks et al., 2017). Data presented here are from the baseline measurement and from judicial documentation of the Ministry of Security and Justice in the Netherlands. It should be noted that as the majority of participants had a criminal record (81%), our research is mainly a study of recidivism in particular, rather than any delinquency. To ensure results are not distorted, we performed analyses on the total sample (N=127), as well as supplemental analyses on only those participants with a criminal record (N=103).

All procedures in the present study were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. The study has been approved by the Medical Ethical Committee of the VU University Medical Center (registration number 2013.422 - NL46906.029.13) and all participants provided written informed consent. Participants received a reimbursement of 30 euros for their participation in the fMRI, ANS, and EEG protocols.

Predictors

We organized baseline variables into four groups: 1) demographics and intelligence; 2) delinquency and drug use; 3) behavioral traits; and 4) neurobiological variables.
The demographics and intelligence category included age, ethnicity (Western, Caribbean, Moroccan, Cape Verdean, Other Non-Western) , education (Primary only, Junior Secondary School, Senior Secondary School), and IQ as measured with four subscales of the Wechsler Adult Intelligence Scale third version (WAIS-III SF; digit symbol coding, information, block design, and arithmetic; Blyler, Gold, Iannone, & Buchanan, 2000).

History of delinquency was assessed as number of past offenses registered in the Research and Policy database Judicial Documentation of the Ministry of Security and Justice in the Netherlands. Years of regular (i.e. weekly) cannabis use and years of regular alcohol use were assessed with the Measurements in the Addictions for Triage and Evaluation Questionnaire (Schippers et al., 2010). Because the data on alcohol use were heavily skewed, we categorized these (0 years, 1-5 years, 6+ years).

Behavioral predictors consisted of reactive aggression and proactive aggression as assessed with the Reactive Proactive Aggression Questionnaire (Cima et al., 2013; Raine, Dodge, Loeber, Gatzke-kopp, Lynam, Reynolds, Stouthamer-loeber, et al., 2006). It is a 23-item self-report measure of aggression scored on a 3-point Likert scale and yields a reactive aggression and a proactive aggression scale. Interpersonal, affective, and behavioral psychopathic traits were assessed with the Youth Psychopathy Inventory – Short Version (van Baardewijk et al., 2010),

which is an 18-item self-report measure scored on a 4-point Likert scale. Internalizing and externalizing problems were assessed with the Adult Self-Report (Achenbach & Rescorla, 2003), which consists of 123 items scored on a 3-point Likert scale.

Autonomic nervous system

Neurobiological predictors including HR and RSA at rest were collected at the Erasmus Behavioral Lab of the Institute for Psychology at the Erasmus University Rotterdam, using the VU Ambulatory Monitoring System (VU-AMS; Klaver, De Geus, & De Vries, 1994). We recorded both an electrocardiogram (ECG) and an impedance cardiogram (ICG) while participants watched a 5-minute excerpt from the video Coral Sea Dreaming (Small World Music Inc.; Piferi, Kline, Younger, & Lawler, 2000). Participants were seated in a comfortable chair in a sound-attenuated room with dimmed lights. Data were processed with the VU-AMS Data, Analysis & Management Software (VU-DAMS). RSA was defined as the longest period between heart beats during expiration minus the shortest period between heart beats during inspiration.

Electrophysiological measures of error processing

ERN and Pe measures of error processing were acquired during the same sessions as the measurements of HR and RSA. In the same room participants performed an Eriksen-Flanker task previously used by Marhe et al. (Marhe, van de Wetering, & Franken, 2013). In short, participants responded to letter strings (HHHHH, SSSSS, HHSHH, SSHSS) by pressing a button with their left or right index finger depending on the middle letter of the string. Each string was presented for 50ms, the maximum response time was 650ms, and a stimulus was shown once every 1450ms. In total 400 trials were presented per participant. The ERN was defined as the difference wave (difference in mean amplitude between correct and incorrect trials) in a 25-100ms post-response window on the FCz electrode. The Pe was defined as the difference wave in a 250-400 post-response window on the Pz electrode (see figure 1). The -100 – 0ms pre-response period was used as baseline. We used a Biosemi ActiveTwo System amplifier to measure the EEG. Silver chloride (Ag/AgCl) electrodes were placed upon the scalp according to the 10-20 International System, with two electrodes on the left and right mastoids as reference. The vertical electro-oculogram horizontal electro-oculogram were assessed to control for ocular artifacts. Signals were digitized with a sampling rate of 512Hz and 24-bit analogue-to-digital conversion, and digitally filtered offline using a low cutoff of 0.15Hz and a high cutoff of 30Hz (24dB/octave slope). Additional artifact rejection (+/-100 μV) was performed automatically.

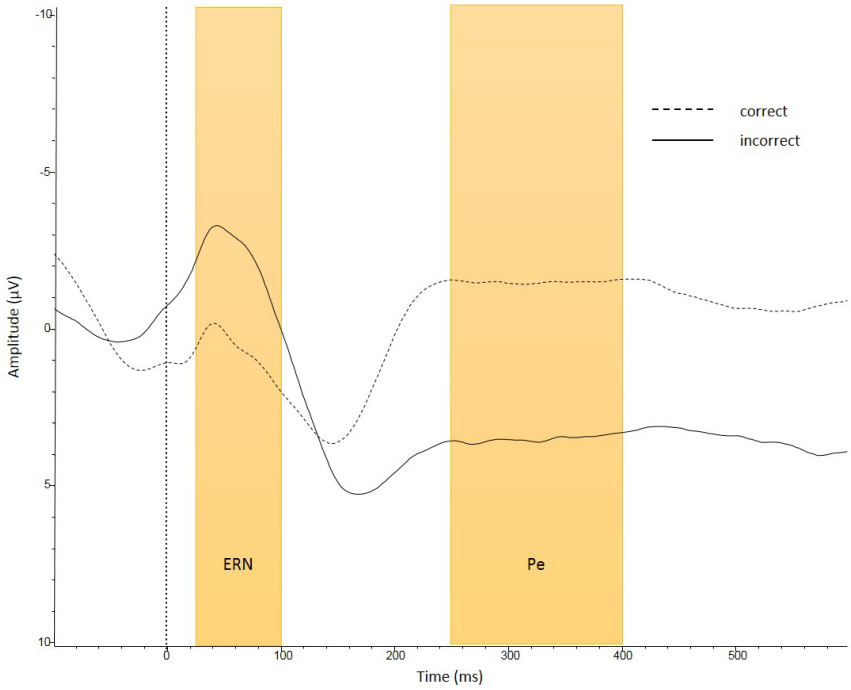


Figure 1. Electroencephalographic waveforms in response to correct and incorrect trials. ERN = error-related negativity; Pe = error positivity.

fMRI measure of inhibition

ACC activity during inhibition was assessed by fMRI. Participants performed a Go-Nogo task previously used by Luijten et al. (Luijten et al., 2013). In short, participants responded to letters (Go trials) presented at 1 Hz, but had to refrain from responding when the letter was the same as the previous one (NoGo trials). In total 817 Go and 110 NoGo trials were presented. ACC activity during inhibition was defined as the brain activity in an a priori defined region of interest (ROI) (14mm radius-sphere at x = 3, y = 24, z = 33; (Aharoni et al., 2013)) during the commission errors vs. correct hits contrast; see figure 2. Data were collected on a 3T GE Healthcare MRI scanner at the Erasmus Medical Center Rotterdam on a different day than the autonomic and EEG measurements. Structural T1-weighted images were acquired with a fast-spoiled gradient pulse sequence in 180 sequential sagittal (S/I) slices, with a thickness of 1.0 mm. The repetition time (TR) was 6.4 ms, the echo time (TE) 2.8 ms, the flip angle (FA) 12 degrees, the field of view (FOV) 240 mm, and the matrix size 240x240 mm. Blood oxygen level-dependent T2*-weighted images were acquired axially (R/L) with an echo planar imaging gradient echo pulse sequence in 42 slices of 3.5 mm with a

slice spacing of 0.5 mm. The TR was 2000ms, the TE 30ms, the FA 80 degrees, the FOV 220 mm, and the matrix size 64x64 mm. Functional imaging data were analyzed using Statistical Parametric Mapping 12 (SPM12; http://www.fil.ion.ucl.ac.uk/spm/). As preprocessing steps, for each participant functional images were realigned and unwarped, the structural scan was segmented and co-registered to the mean T2*-weighted image. Images were then normalized to the MNI template and smoothed with an 8mm full-width half maximum Gaussian filter. We modelled four conditions and added six movement parameters as covariates of no interest. We extracted ROI data using the Marsbar toolbox for SPM (http://marsbar.sourceforge.net/).

Outcome

Information on two outcome measures was assessed during follow-up. The first outcome measure is time to arrest for any criminal offense. This includes – as defined by the Research and Documentation Centre of the Ministry of Security and Justice in the Netherlands – both relatively minor offenses (e.g. resistance, drunk

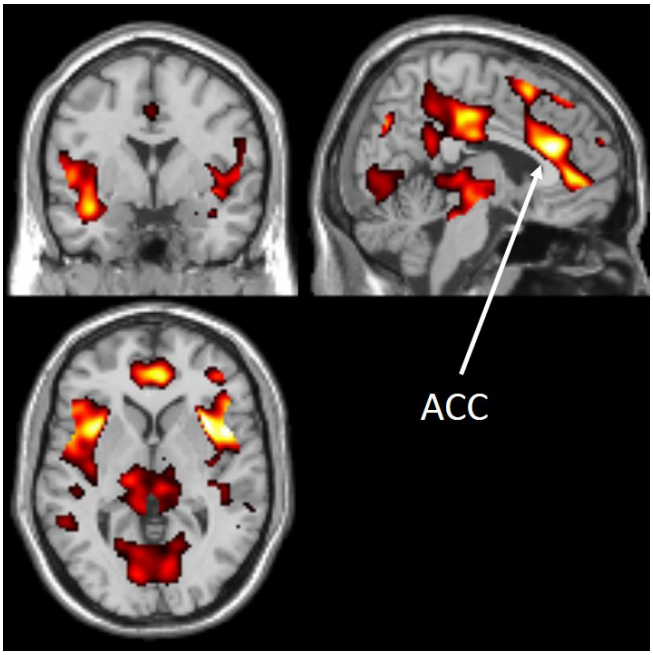


Figure 2. Whole brain family wise error corrected hemodynamic activity during the commission errors vs. correct hits contrast, x = 49, y = 64, z = 38. ACC = anterior cingulate cortex.

driving, possession of a weapon) and serious offenses (i.e. those with a minimum 4-year sentence, e.g. assault, aggravated theft, rape; Wartna, Blom, & Tollenaar, 2011). The second outcome measure is time to arrest for serious offenses alone. Data were obtained from the Research and Policy database Judicial Documentation of the Ministry of Security and Justice in the Netherlands, and included arrests from baseline measurement until January 2018. The median follow-up time was 31 months (range = 14-47).

Data analysis

We imputed to 40 complete data sets (White, Royston, & Wood, 2011) using IBM SPSS 21 for variables with a maximum missingness of 30%; no outcomes were imputed. First, we performed Cox proportional hazard models to assess potential predictors adjusting for age for each of the two outcomes. We selected all variables that were significant at a $p < .10$ level in the model for any offense or serious offenses to be included in the fully adjusted Cox models; we use a liberal value of $p < .10$ because use of a more traditional level of $p < .05$ often fails to identify important variables (Hosmer & Lemeshow, 2000). We tested the proportional hazard assumption by testing the associations between Schoenfeld residuals (Schoenfeld, 1982) and time. We standardized all effect sizes except for age. Second, using the risksetROC package (Heagerty & Zheng, 2005) in R 3.5.1 we calculated (areas under) time-dependent receiver operating characteristic (ROC) curves to compare the predictive performance of the different variable groups over time and to assess whether adding variable groups increased predictive performance above simpler models that included less variables. Time-dependent ROC curves represent the relationship of time-dependent sensitivity and specificity and the areas under the ROC curves (AUC) measure the probability that the predictive value for a randomly selected offender exceeds the predictive value for a randomly selected non-offender. Finally, we computed C-indexes for 6, 12, 18, 24, and 30-month prediction, which is the concordance statistic over a time-period based on the weighted averages of the AUCs. It represents the predictive ability of determinant blocks, with a C-index above 0.70 indicating a good model and a C-index above 0.80 indicating a strong model (Hosmer & Lemeshow, 2000).

Results

Of the 127 participants, in the follow-up period 61 (48.0%) were arrested for any offense, of which 36 (28.3% of total) were arrested for a serious offense. In the age adjusted models the following variables predicted both any and serious offenses: past offenses, cannabis use, reactive aggression, proactive aggression, HR, and ERN. In contrast, ethnicity (Moroccan vs. Western and Cape Verdean vs. Western) predicted

Table 1. Descriptives and univariate Cox regressions

	Baseline	General offenses		Serious offenses	
	Mean (SD)/N (%)	RR (95%-CI)	p	RR (95%-CI)	p
Demographics and intelligence					
Age	21.98 (2.4)	1.01 (0.91-1.13)	0.846	0.94 (0.81-1.08)	0.365
Ethnicity					
Western	22 (17.3)		ref		ref
Caribbean	55 (43.3)	1.98 (0.82-4.78)	0.131	1.70 (0.57-5.05)	0.342
Moroccan	21 (16.5)	2.70 (1.02-7.13)	0.045	2.07 (0.62-6.87)	0.237
Cape Verdean	8 (6.3)	2.78 (0.89-8.69)	0.078	1.30 (0.24-7.15)	0.763
Other non-western	21 (16.5)	1.29 (0.44-3.72)	0.644	1.19 (0.32-4.44)	0.796
Education					
Senior secondary	23 (18.1)		ref		ref
Junior secondary	48 (37.8)	1.15 (0.54-2.45)	0.721	0.62 (0.23-1.67)	0.348
Primary	56 (44.1)	1.45 (0.69-3.04)	0.332	1.09 (0.44-2.71)	0.852
IQ	82.07 (10.2)	0.82 (0.64-1.07)	0.144	0.86 (0.61-1.22)	0.402
Delinquency and drug use					
Past offenses (amount)	5.06 (0.06)	1.51 (1.27-1.79)	<.001	1.72 (1.40-2.10)	<.001
Cannabis use (years)	4.28 (3.83)	1.27 (0.98-1.65)	0.069	1.43 (0.93-2.05)	0.051

Table 1. (cont.) Descriptives and univariate Cox regressions

	Baseline	General offenses		Serious offenses	
	Mean (SD)/N (%)	RR (95%-CI)	p	RR (95%-CI)	p
Delinquency and drug use					
Alcohol use					
0 years	73 (57.5)		ref		ref
1-5 years	31 (24.4)	0.88 (0.45-1.71)	0.965	0.93 (0.40-2.15)	0.863
6+ years	23 (18.1)	0.81 (0.40-1.65)	0.569	0.90 (0.34-2.37)	0.836
Behavior					
Reactive aggression	11.28 (4.65)	1.53 (1.17-2.00)	0.002	1.57 (1.11-2.22)	0.011
Proactive aggression	5.28 (4.28)	1.38 (1.10-1.72)	0.005	1.47 (1.12-1.93)	0.005
Psychopathy - Interpersonal	11.27 (3.86)	0.90 (0.70-1.15)	0.384	1.07 (0.79-1.46)	0.659
Psychopathy - Affective	10.83 (3.51)	1.04 (0.82-1.31)	0.776	1.13 (0.83-1.53)	0.440
Psychopathy - Behavioral	12.21 (3.14)	1.07 (0.83-1.38)	0.595	1.38 (1.00-1.89)	0.047
Internalizing problems	72.52 (24.19)	0.99 (0.77-1.27)	0.924	0.91 (0.66-1.26)	0.571
Externalizing problems	69.22 (23.83)	1.07 (0.82-1.40)	0.627	1.17 (0.82-1.69)	0.386
Neurobiology					
Heart rate	65.78 (9.11)	0.70 (0.52-0.93)	0.014	0.53 (0.35-0.79)	0.002
Respiratory Sinus Arrhythmia	95.70 (42.48)	1.17 (0.94-1.46)	0.165	1.22 (0.91-1.64)	0.177
Error-related negativity	-5.17 (4.72)	1.47 (1.10-1.96)	0.008	1.53 (1.05-2.25)	0.029
Positivity error	6.13 (5.07)	0.83 (0.64-1.08)	0.168	0.70 (0.49-0.99)	0.043
Anterior cingulate cortex activity	2.87 (2.34)	1.05 (0.81-1.36)	0.741	1.27 (0.90-1.80)	0.179

Table 2. Full cox models for general and serious offenses in total sample (N=127)

	General offenses		Serious offenses	
	RR (95%-CI)	p	RR (95%-CI)	p
Demographics and intelligence				
Age	0.98 (0.86-1.12)	.788	0.88 (0.74-1.05)	.150
Ethnicity				
Western		ref		ref
Caribbean	2.25 (0.86-5.93)	.100	1.71 (0.53-5.57)	.370
Moroccan	3.07 (1.04-9.10)	.043	2.07 (0.55-7.81)	.284
Cape Verdean	2.65 (0.73-9.69)	.140	0.75 (0.10-5.50)	.779
Other non-western	1.62 (0.52-5.08)	.407	1.27 (0.29-5.54)	.749
Delinquency and drug use				
Past offenses (amount)	1.45 (1.17-1.79)	< .001	1.71 (1.33-2.23)	< .001
Cannabis use (years)	1.21 (0.90-1.63)	.200	1.39 (0.92-2.09)	.120
Behavior				
Reactive aggression	1.26 (0.87-1.81)	.223	0.95 (0.60-1.52)	.836
Proactive aggression	1.01 (0.72-1.42)	.944	1.07 (0.70-1.62)	.761
Psychopathy - Behavioral	1.08 (0.78-1.50)	.630	1.54 (1.00-2.36)	.049
Neurobiology				
Heart rate	0.88 (0.65-1.19)	.389	0.62 (0.38-0.99)	.023
Error-related negativity	1.61 (1.13-2.28)	.008	1.52 (0.96-2.40)	.075
Positivity error	0.93 (0.69-1.26)	.650	0.75 (0.49-1.16)	.269

Table 3. Full Cox models for general and serious offenses in subsample (N=103)

	General offenses		Serious offenses	
	RR (95%-CI)	p	RR (95%-CI)	p
Demographics and intelligence				
Age	0.95 (0.82-1.09)	.460	0.85 (0.70-1.02)	.072
Ethnicity				
Western		ref		ref
Caribbean	1.71 (0.64-4.56)	.281	1.40 (0.43-4.57)	.573
Moroccan	2.03 (0.66-6.22)	.217	1.53 (0.40-5.90)	.539
Cape Verdean	2.03 (0.55-7.46)	.288	0.73 (0.10-5.18)	.755
Other non-western	0.96 (0.28-3.34)	.947	1.20 (0.27-5.42)	.813
Delinquency and drug use				
Past offenses (amount)	1.37 (1.09-1.72)	.007	1.67 (1.27-2.19)	< .001
Cannabis use (years)	1.04 (0.77-1.41)	.801	1.27 (0.83-1.93)	.273
Behavior				
Reactive aggression	1.15 (0.78-1.69)	.497	0.92 (0.57-1.49)	.735
Proactive aggression	1.11 (0.77-1.60)	.581	1.08 (0.69-1.67)	.747
Psychopathy - Behavioral	1.17 (0.83-1.64)	.375	1.56 (1.00-2.44)	.049
Neurobiology				
Heart rate	0.84 (0.61-1.14)	.260	0.57 (0.36-0.90)	.016
Error-related negativity	1.95 (1.29-2.96)	.002	1.66 (1.01-2.73)	.046
Positivity error	1.06 (0.77-1.47)	.710	0.76 (0.48-1.22)	.256

only any offenses, whereas behavioral psychopathic traits and the Pe predicted only serious offenses. See table 1 for full results with effect estimates. We included these nine predictors in the mutually adjusted models retaining age as a covariate. In the final model for any offense three predictors were significantly related to any offending: ethnicity Moroccan vs. Western ($p < .05$, RR = 3.07, CI = 1.04-9.10), past offenses ($p < .001$, RR = 1.45, CI =1.17-1.79), and a smaller ERN ($p < .05$, RR = 1.49, CI = 1.09-2.03); see table 2. Likewise, in the final model for serious offenses three predictors were significantly related to serious offending: past offenses ($p < .001$, RR = 1.71, CI = 1.33-2.23), behavioral psychopathic traits ($p < .05$, RR = 1.54, CI = 1.00-2.36), and low HR ($p < .05$, RR = 0.62, CI = 0.38-0.99); see table 2. In the supplemental analysis on the subgroup with a criminal record (N=103), results were similar, albeit ethnicity failed to reach significance, and ERN reached significance ($p = .046$, compared to $p = .075$); see table 3).

Any offense

For each of the four variable groups we calculated AUCs for different time points as a measure of the predictive power over time. Figure 3 shows that AUCs for all groups of variables is fairly stable over time. The neurobiological measures and delinquency and cannabis use perform best (C30month = 0.64), the behavior group performs similarly (C30 = 0.63) and age and ethnicity perform worst (C30 = 0.57); see table 4. In Figure 4 we show the predictive power of models stepwise including more variable groups. The figure demonstrates that the neurobiological measures add to the predictive power above all other variables, and that this added predictive power slightly decreases over time. The model without neurobiological measures performs moderately well (C30 = 0.68), yet adding neurobiological measures increased the predictive power (C30 = 0.72). Results of the supplemental analysis on the subgroup with a criminal record are very similar, with identical C-indexes for the complete model (see table 5).

Serious offenses

Figure 5 shows the predictive power of the variable groups over time, which is again fairly stable for each variable group. Table 4 shows that neurobiological measures (C30 = 0.70) and delinquency and cannabis use (C30 = 0.68) outperform demographic (C30 = 0.60) and behavioral measures (C30 = 0.64). Figure 6 demonstrates that the neurobiological predictors consistently add predictive power above the other variables. The model without neurobiological predictors performs well (C30 = 0.75), yet again adding neurobiological measures increased the predictive performance (C30 = 0.80). Results of the supplemental analysis on the subgroup with a criminal record are very similar, with identical C-indexes for the complete model (see table 5).

Discussion

In this study, we showed that in a sample of delinquent individuals, models including demographic variables, delinquency and drug use, behavioral traits, and neurobiological variables predicted overall and in particular serious recidivism well. This is the first study to assess the combined and independent predictive value of several multimodal neurobiological measures: resting HR and RSA, two EEG measures

Table 4. C-indexes for different time intervals in full sample (N=127)

		Months				
		6	12	18	24	30
General offenses						
Group	Age and Ethnicity	0.57	0.57	0.57	0.57	0.57
	Delinquency and Cannabis Use	0.65	0.65	0.64	0.64	0.64
	Behavior	0.63	0.63	0.63	0.63	0.63
	Neurobiology	0.65	0.65	0.65	0.65	0.64
Model	Age and Ethnicity	0.57	0.57	0.57	0.57	0.57
	Age and Ethnicity + Delinquency and Cannabis Use	0.68	0.67	0.67	0.67	0.67
	Age and Ethnicity + Delinquency and Cannabis Use + Behavior	0.69	0.69	0.69	0.68	0.68
	Age and Ethnicity + Delinquency and Cannabis Use + Behavior + Neurobiology	0.74	0.73	0.73	0.72	0.72
Serious offenses						
Group	Age and Ethnicity	0.60	0.60	0.60	0.60	0.60
	Delinquency and Cannabis Use	0.69	0.69	0.69	0.69	0.68
	Behavior	0.64	0.64	0.64	0.64	0.64
	Neurobiology	0.70	0.70	0.70	0.70	0.70
Model	Age and Ethnicity	0.60	0.60	0.60	0.60	0.60
	Age and Ethnicity + Delinquency and Cannabis Use	0.74	0.74	0.74	0.74	0.74
	Age and Ethnicity + Delinquency and Cannabis Use + Behavior	0.76	0.76	0.76	0.75	0.75
	Age and Ethnicity + Delinquency and Cannabis Use + Behavior + Neurobiology	0.82	0.81	0.81	0.81	0.80

Table 5. C-indexes for different time intervals in subsample (N=103)

		Months				
		6	12	18	24	30
General offenses						
Group	Age and Ethnicity	0.57	0.57	0.57	0.57	0.57
	Delinquency and Cannabis Use	0.61	0.60	0.60	0.60	0.60
	Behavior	0.61	0.61	0.60	0.60	0.60
	Neurobiology	0.66	0.66	0.66	0.66	0.65
Model	Age and Ethnicity	0.57	0.57	0.57	0.57	0.57
	Age and Ethnicity + Delinquency and Cannabis Use	0.65	0.64	0.64	0.64	0.64
	Age and Ethnicity + Delinquency and Cannabis Use + Behavior	0.67	0.67	0.66	0.66	0.66
	Age and Ethnicity + Delinquency and Cannabis Use + Behavior + Neurobiology	0.74	0.73	0.73	0.72	0.72
Serious offenses						
Group	Age and Ethnicity	0.62	0.62	0.62	0.61	0.61
	Delinquency and Cannabis Use	0.65	0.65	0.65	0.65	0.65
	Behavior	0.63	0.62	0.62	0.62	0.62
	Neurobiology	0.69	0.69	0.69	0.70	0.70
Model	Age and Ethnicity	0.62	0.62	0.62	0.61	0.61
	Age and Ethnicity + Delinquency and Cannabis Use	0.72	0.72	0.72	0.72	0.72
	Age and Ethnicity + Delinquency and Cannabis Use + Behavior	0.75	0.74	0.74	0.74	0.73
	Age and Ethnicity + Delinquency and Cannabis Use + Behavior + Neurobiology	0.82	0.81	0.81	0.80	0.80

of error processing, and an fMRI measure of inhibition. We found three of these neurobiological measures to be associated longitudinally with criminal recidivism in age-adjusted analyses, and more importantly, these measures had incremental predictive value above traditional risk factors.

Although a wide array of variables univariately predicted recidivism, understandably most predictors failed to reach significance in the final, mutually adjusted models. Delinquency is a complex multi-factorial phenomenon and no single variable reliably predicts recidivism with the exception of the number of past offenses.

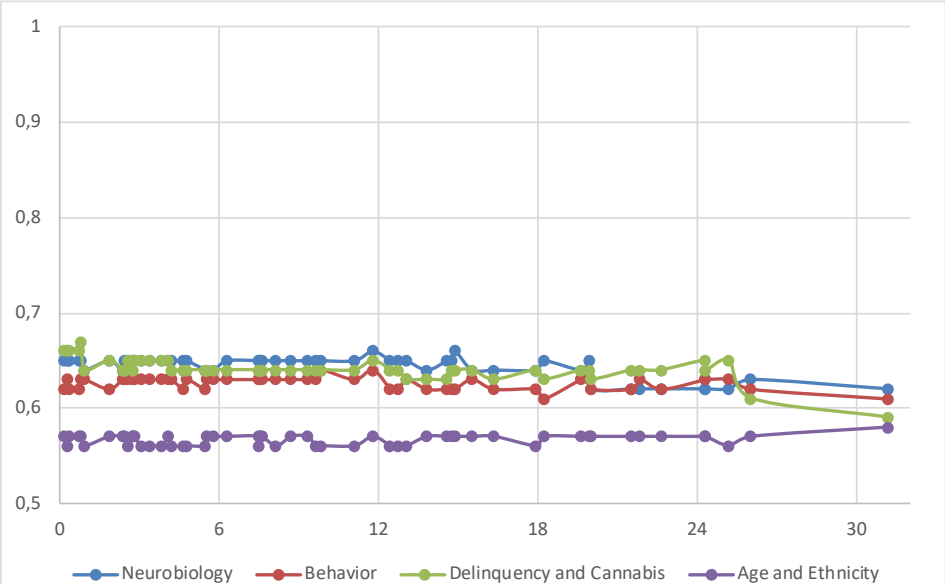


Figure 3. Areas under time-dependent receiver-operating characteristic curves for prediction of general offenses for different variable groups

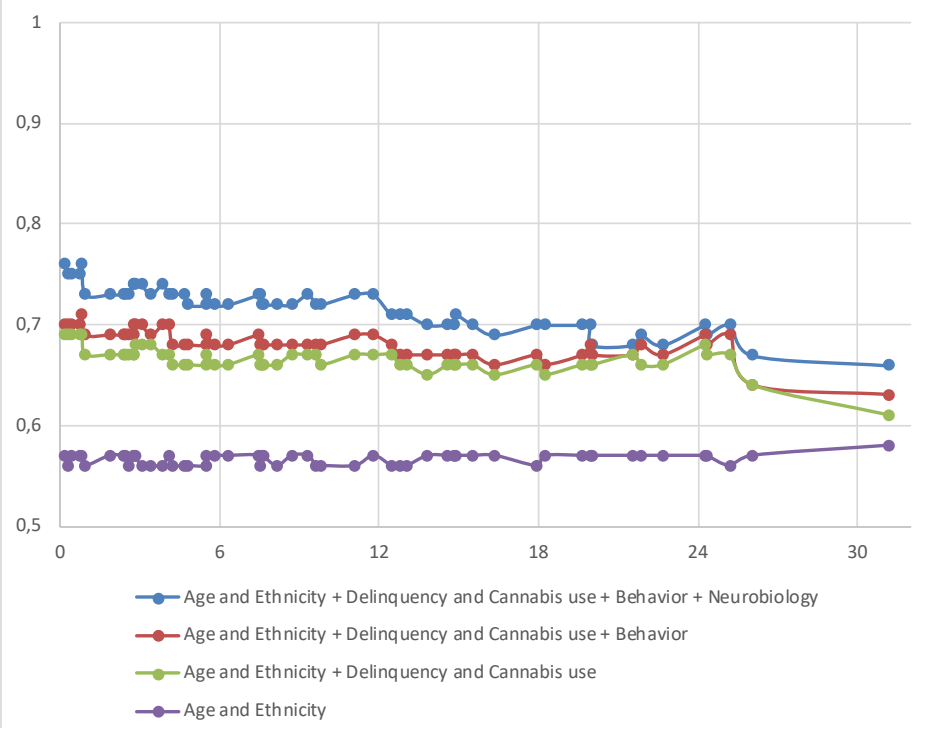


Figure 4. Areas under time-dependent receiver-operating characteristic curves for prediction of general offenses for different models

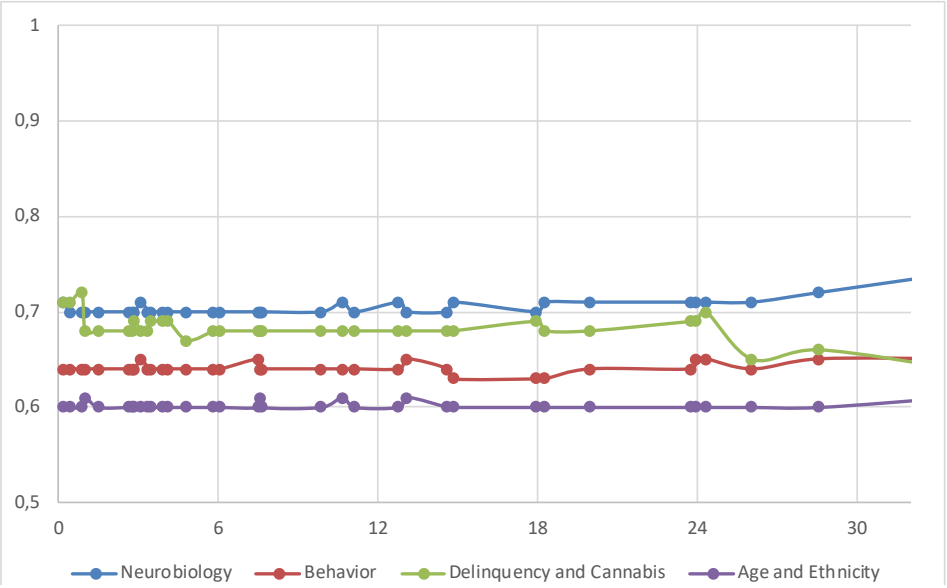


Figure 5. Areas under time-dependent receiver-operating characteristic curves for prediction of serious offenses for different variable groups

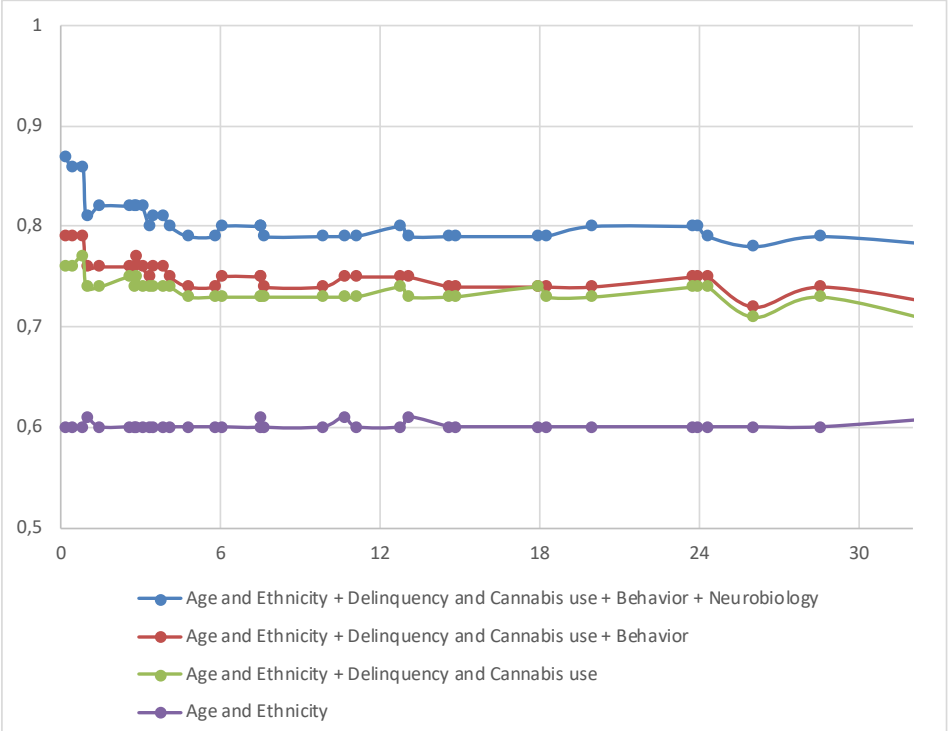


Figure 6. Areas under time-dependent receiver-operating characteristic curves for prediction of serious offenses for different models

Low resting HR predicted serious recidivism, which is in line with low arousal and fearlessness theory (Raine, 1993). Another previous study found a similar association that was stronger for violent than nonviolent crimes (Latvala et al., 2015). Behavioral psychopathic traits also independently contributed to the prediction of serious recidivism. Concerning overall recidivism, the ERN was the only additional significant predictor, with a smaller ERN – indicating diminished early error processing – related to increased recidivism. Although the ERN measure failed to reach significance in the model of serious recidivism, effect sizes in both models were very similar (RR = 1.61 for overall recidivism and RR = 1.52 for serious recidivism). In the study by Steele et al. (2015), the ERN was not found to be predictive of recidivism, but this study is limited by its small sample size (N=45). In line with findings that a smaller ERN is related to antisocial behavior in general (Hall et al., 2007), our results suggest that the inability to adequately process adverse consequences may underlie the continuation of criminal behavior despite its negative consequences.

In contrast with a previous study (Aharoni et al., 2013), we did not find an association between inhibitory ACC activity and recidivism. As we employed a very similar task and found expected brain activity it seems unlikely that we measured a different process. Possibly, the difference is due to variation between investigated samples. Aharoni et al. (Aharoni et al., 2013) studied incarcerated offenders with a large age range (20-52 years) who performed the task before being released from prison, whereas our sample consisted of young adults (18-27 years) who were not incarcerated. It may be that the relevance of inhibitory processes for delinquent behavior increases with age or that the setting of the experiment influenced results. It should also be taken into account that replication of fMRI findings has proven to be difficult (Bennett & Miller, 2010), complicating the interpretation of discrepant results. Concerning the Pe, although it did not reach significance in the mutually adjusted models, we did find that a smaller Pe univariately predicts serious recidivism and the effect size remained similar in the full model. This is in line with research finding associations between a smaller Pe and antisocial behavior in adolescents (16-20 years; Maurer et al., 2015), but at odds with findings by Steele et al. (Steele, Claus, et al., 2015) who found a larger Pe to be predictive of rearrest in a sample of 45 incarcerated adults. Again, the age differences between participant groups may be a relevant factor in explaining these discrepancies.

For both overall and serious recidivism, the neurobiological measures had a greater predictive value than the other groups of variables, and importantly, they improved the predictive performance of the models without neurobiological measures. Although our study warrants extension and replication, our low HR finding is in accordance with theory and previous research in both population-based and at-risk samples, bolstering the idea that HR can be a reliable indicator of future delinquency. Concerning EEG and MRI measures, based on the available studies it

cannot definitively be concluded which measures of executive functioning have greater predictive potential, but there are considerable practical advantages of using EEG rather than fMRI measures: the former is relatively cheap, less time consuming, technically relatively easy to acquire, and less invasive. Measurements of the autonomic nervous system enjoy the same benefits. Overall, our findings suggest that adding neurobiological measures to risk assessments may be a viable way to improve the predictive accuracy of recidivism. However, currently too little data are available to justify implementing this type of risk assessment in judicial practice, and studies in more regulated environments such as prisons are warranted to assess the practical utility of such risk assessment. Additionally, future research would benefit from larger sample sizes and longer follow-up periods to assess whether prediction is stable across time, and whether neurobiological measures are truly viable as risk-factors (for a discussion see Poldrack et al., 2018).

In sum, we found that a group of three multimodal neurobiological measures adds to the prediction of overall and serious recidivism above demographic and behavioral measures. As the most feasible measures, autonomic functioning and electroencephalography, are also most predictive, in the future they may be viable to be included in risk assessment.

Chapter 7:
Summary and general discussion

The general aim of this dissertation was to increase our understanding of the neural correlates of several antisocial traits in multi-problem young adults, and to assess whether such neurobiological measures could be used to increase the prediction of criminal recidivism. Specifically, in a large sample of multi-problem young adult men (N = 127, age 18 to 27; drawn from a larger sample of 696 multi-problem young adults), we collected functional magnetic resonance imaging data, electroencephalographical data, and data on the autonomic nervous system (ANS) to assess neurobiological functioning across different measurement techniques. We investigated how affective callous-unemotional, impulsive and irresponsible, and grandiose-manipulative interpersonal psychopathic traits, and reactive and proactive aggression within this population are associated with three pertinent processes relevant to these issues: moral evaluation, cognitive control, and autonomic nervous system functioning. In this final chapter, results of the empirical chapters, scientific and practical implications, and suggestions for future research will be discussed.

Multi-problem young adults compared to healthy controls

The control group was age and gender group-matched to the multi-problem young adults and selected to have average education. Although the main purpose of the inclusion of this control group was to assess task validity of the experimental paradigms, comparing the control participants to the multi-problem young adults gave additional insights into the difficulties multi-problem young adults present with.

We found that multi-problem young adults perform worse than controls on various measures. First, in their moral evaluation of situations (chapter 3) they were capable of differentiating between immoral situations and nonmoral (but still negative) situations, but did so less well than controls. Whereas they rated neutral situations the same as controls (i.e. not immoral), they judged immoral situations to be less immoral than controls did and judged nonmoral situations to be more immoral than controls did. Second, their performance during a cognitive control task (chapter 4) was worse than controls, their accuracy on the task was significantly lower than that of controls (81% versus 87% respectively). In contrast, their assessment of emotions during sad film clips (chapter 5) did not differ from controls. They recognized that the boys in the film clips were sad and similar to controls they identified some degree of fear and anger. However, controls showed no variation whatsoever in their assessment of happiness (each control participant rated no happiness at all), while some multi-problem young adults also identified some degree of happiness. This may indicate some uncertainty in the multi-problem group with regard to the recognition of positive emotions, but this is not possible to assess accurately with the current data.

We found only few differences between multi-problem young adults and controls on the neurobiological measures we assessed. During moral evaluation (chapter 3), the groups showed similar neural activity throughout the brain and this pattern of activation of both groups was consistent with brain areas implicated in moral evaluation by previous research (most relevant are the ventromedial prefrontal cortex and superior temporal gyrus; (Garrigan et al., 2016). Likewise, both the functioning of the autonomic nervous system in rest and the reactivity of the autonomic nervous system to sadness (chapter 5) showed no differences between the groups on any of the assessed measures (i.e. heart rate, respiratory sinus arrhythmia, pre-ejection period, and skin conductance level). We did find differences between multi-problem young adults and controls on one of the neural measures of error processing. Multi-problem young adults had significantly smaller early brain responses to errors, as measured with the error-related negativity, indicating decreased automatic error processing. The later, more conscious processing of errors, as measured with the error positivity, was not affected in multi-problem young adults. Overall, deficits in executive functioning are in line with the literature on antisocial behavior (Ogilvie, Stewart, Chan, & Shum, 2011). Specifically, decreased neural early error processing may underlie the persistence of disruptive behavior as errors may be perceived or experienced as less meaningful (Hajcak et al., 2005).

A possible explanation for the diminished differentiation between moral and nonmoral events, lesser performance on the error processing task, and decreased neural early error processing is the level of intelligence of the population. Although we did not assess IQ in the control group, we selected them to have average education level and assume they have average IQs, whereas the multi-problem group has a low average IQ of 83. Additionally, we found IQ to be significantly related to the rating of nonmoral stimuli ($r = -.41$), to accuracy on the error processing task ($r = .32$), and to the error-related negativity ($r = -.19$). In all cases IQ was related to better performance. However, the comparison of multi-problem young adults to controls is complicated by several factors. First, the size of the control group was fairly small (N=27), limiting power of the group analyses and one of the major reasons why findings should be viewed as explorative. Second, multi-problem young adults are a heterogeneous group of people; there exists great variation in the problems they present with. Therefore, it is hard to assess to what characteristics the differences (and similarities) in behavioral and biological functioning between the groups can be attributed. For example, they could be due to differences in externalizing problems, differences in childhood adversity, or differences in drug use. However, it is also possible that subgroups of multi-problem young adults suffer from different combinations of problems and that they perform similar to controls on average, but that different clusters of multi-problem young adults present with variant aberrant functioning. It is important to realize this can only be studied if research into multi-problem young

adults is embedded in a large, population-based study, because as they suffer from multiple, interrelated problems there exists no control group that varies on only a single or a few parameters. In chapter 2 we showed through cluster analysis that the behavior of multi-problem young adults indeed clusters within profiles that differ according to the severity and nature of problems, but unfortunately neurobiological data on too few participants (127 of 696 participants) was available to assess whether these clusters also differed in neurobiological functioning. Such research on a larger scale may shed light on the diversity of findings in different antisocial samples.

Neural correlates of antisocial behaviors within multi-problem young adults

Dimensional analyses in which three psychopathic traits (chapters 3 and 4) or three psychopathic traits and two types of aggression (chapter 5) were employed as independent variables revealed limited associations between antisocial behaviors and neurobiological functioning. We found relationships between psychopathy and brain activity during moral evaluation in several brain areas (chapter 3). Specifically, the callous-unemotional trait of psychopathy was related to increased brain activity in three a priori regions of interest: the left ventromedial prefrontal cortex, the left superior temporal gyrus, and the left cingulate gyrus. For both measures of neural error processing (chapter 4) and for baseline activity and reactivity of the autonomic nervous system (chapter 5) we found no relations between any of the antisocial behaviors and neurobiological measures.

Our findings on the moral evaluation task suggest that the affective callous-unemotional traits of psychopathy may be related to widespread altered activation patterns during moral evaluation, rather than more exclusively to the ventromedial prefrontal cortex and amygdala as is suggested by theory (Blair, 2007). Other studies have found negative relations between amygdala activity and psychopathy in moral paradigms, but only in contrast with neutral stimuli (i.e. immoral + nonmoral > neutral, immoral > neutral, and nonmoral > neutral contrasts) (Harenski, Edwards, et al., 2014a; Harenski, Harenski, et al., 2014; Harenski et al., 2010). A limitation to analysis of these contrasts is that it includes the valence (i.e. negative affect) as well as the moral value of stimuli, rather than the moral value alone. This complicates the interpretation of the association between psychopathy and brain activity, because the association may be due the valence, the moral value, or both. It may be the case that amygdala dysfunction is relevant to moral processing, exactly because it is involved in an affective processing component that is required to make moral evaluations. For example, if moral evaluation would (partially) be driven by the feeling that something is wrong. Alternatively, it is possible that moral assessment

does not require affective processing, but the two are correlated because immoral acts have negative valence for most people. Finally, in psychopathy the affective process could be less relevant to moral assessment. Which explanations fits best requires more specific research, but results from one study in community volunteers do suggest that amygdala involvement varies with how emotional the evaluated moral situations are and that in psychopathy the amygdala involvement is less (Glenn et al., 2009a).

Regarding error processing, our results add to the existing evidence that neural early error processing is intact in psychopathy (e.g. Brazil et al., 2009; Maurer et al., 2015, 2018), but the null-findings across all three psychopathic factors for neural late error processing are harder to interpret. One explanation could be that initial error-processing deficits in adolescence (where a negative association between late error processing and psychopathy was found previously (Maurer et al., 2015) change into error-processing overcompensation in adulthood (where a positive association between late error processing and psychopathy has been reported (Steele, Maurer, et al., 2015). If so, our young adult sample may find itself in this transition. Another possibility is that the null-finding is due to the use of a self-report measure of psychopathy. One study that compared self-report measures to an interview-based instrument found a negative relation between neural late error processing and psychopathy as assessed by interview, but not as assessed by four different self-report questionnaires (Maurer et al., 2018).

Likewise, our null-findings for the autonomic nervous system measures in relation to all antisocial measures are somewhat puzzling, as aberrant baseline autonomic activity is a robust finding in studies of antisocial behavior (e.g. Lorber, 2004; Ortiz & Raine, 2004; Portnoy & Farrington, 2015). This may partly be explained by the fact that effect sizes in adults are approximately twice as small as in children (Portnoy & Farrington, 2015) and thus harder to detect. Of course, it is also possible that within multi-problem young adults no relation between antisocial behaviors and functioning of the ANS exists. This may be the case if aberrant autonomic functioning would be present specifically in particular subgroups with more or less extreme levels of antisocial behavior. However, as similar relations between ANS activity and antisocial behaviors are present in community samples as well as clinical samples varying between individuals with behavioral disorders and psychopathic offenders (Portnoy & Farrington, 2015) this does not seem likely. Moreover, in chapter 5 we showed that baseline heart rate is predictive of criminal recidivism longitudinally within multi-problem young adults (also see paragraph 'Neuroprediction' below), indicating that within our sample it is related to criminal behavior regardless of the fact that it is not related to psychopathy or aggression.

There are several limitations to be considered with regards to our dimensional findings. First, as multi-problem young adults comprise a highly antisocial sample,

there is a risk that within the group there exists too little variation on the psychopathy and aggression measures or that relatively much of the variation is measuring error rather than true variation. However, as the individual scores on the measures span the entire range, this does not seem likely. In fact, contrary to expectation, our sample of multi-problem young adults has similar psychopathy scores as the admittedly small control group. Therefore, one concern was whether the Youth Psychopathy Inventory (YPI) was appropriate to use in multi-problem young adults. In chapter 4, we showed through confirmatory factor analysis and supporting tests for external validity that it is a valid instrument in our sample.

Second, the manner in which psychopathy was assessed makes it difficult to compare to other research. Whereas a large proportion of studies employ the Psychopathy Checklist – Revised or the Psychopathy Checklist Youth Version (Hare, 2003), that include data from an extensive interview as well as record data, we used the YPI (van Baardewijk et al., 2010), which is a self-report measure of psychopathy. Although the conceptualizations of psychopathy of different instruments overlap, there are some noteworthy differences between various measures. Most importantly, whether criminal behavior is viewed as part of the psychopathic construct (Hare & Neumann, 2008) or as a common consequence of psychopathy (Cooke & Michie, 2001). In the YPI, criminal behavior is not included in the definition and thus will not capture associations with that behavior. This may partly explain why we have not found associations between the YPI and EEG and ANS measures (chapters 3 and 4), but have found EEG and ANS measures to be predictive of future delinquency (chapter 5, also see next paragraph).

Neuroprediction of delinquency

In chapter 5, we investigated the incremental predictive value of neurobiological measures over and above known risk factors for general and serious criminal recidivism within multi-problem young adults. From the known risk factors, we found number of past offenses, proactive and reactive aggression, and the behavioral psychopathic factor to be good individual predictors. From the neurobiological measures, we found baseline heart rate, the error-related negativity (ERN), and the positivity error (Pe) to be good individual predictors. In the full models, this group of three neurobiological variables increased predictive power over and above demographical and behavioral measures. Particularly, in the analysis of serious recidivism these measures improved the predictive function.

Our findings are in line with previous research showing that baseline heart rate is a strong predictor of violent delinquency (Latvala et al., 2015). The only other study that assessed the predictive value of EEG measures of error processing found

no effect for the ERN and a larger Pe to predict delinquency in adult offenders (mean age = 32.7; Steele, Claus, et al., 2015). In contrast, we found a smaller ERN and a smaller Pe to predict recidivism in young adults, which is in line with the idea that diminished error processing, as reflected by decreased neural reactivity, can lead to the repetition of problem behavior. As with our divergent findings on the relation between psychopathy and the Pe, this is possibly due to the age differences between studied samples. Following an earlier study, where activity in the anterior cingulate (ACC) during an inhibitory Go-Nogo task was found (Aharoni et al., 2013), we included ACC activity from the same region of interest during a similar Go-Nogo task, but did not replicate the finding. Before implications from this study are discussed below under 'Scientific implications and future research', I will first argue why a clear distinction between practical and scientific implications is essential in scientific research.

On practical implications from cross-sectional and neurobiological research

In my view, the practical (e.g. clinical and judicial) implications that can be confidently drawn from cross-sectional research in general and neurobiological cross-sectional research specifically are limited. Single cross-sectional studies are useful tools in prevalence assessment, hypothesis formation, and hypothesis testing, and as such may results in scientific or theoretical implications (i.e. implications for scientific research and implications for scientific models). However, they do not contribute meaningfully to the evidence for causality and cannot help better estimate prognosis (Rothman, Greenland, & Lash, 2012). As such, cross-sectional studies shed little light on what should be done in practice. Nonetheless, clinical implication sections are common in cross-sectional papers, sometimes demanded by journals and for grant applications, and I have yet to attend a conference talk discussing cross-sectional neurobiological research after which there was *no* question regarding clinical implications. Although I believe translating research findings into daily practice is an essential part of science, I argue that researchers should be more aware of the limitations of what follows and can (not) follow from their data (see e.g. Ioannidis, 2005). Overinterpretation of results can lead to incorrect conclusions, cumulative bad science, and unfounded and potentially harmful recommendations. Let me exemplify the issue with a fictional situation.

Suppose a researcher naïve to osteoarthritis, of which the initial major symptom is erosion of cartilage, performs research in people with knee pain. He assesses a hundred participants with knee pain and a hundred group-controlled participants without knee pain, gathers x-ray and magnetic resonance imaging data on their knees, and concludes that the cartilage in the knee joints of the participants

with knee pain is significantly more eroded than that of the controls. The researcher may sensibly reason that as the cartilage is affected, treatment should be focused on strengthening the cartilage that is left or regaining the cartilage that is lost, and the researcher may incorporate these ideas in his scientific paper as clinical implications. However, such a treatment would have minor, if any, effect, because cartilage does not regenerate well. Rather, treatment should be focused on strengthening surrounding muscle tissue, so that it can lighten the load on the cartilage. It is not that the researcher's reasoning is unsound per se given his findings, but his suggestions are of a speculative or hypothetical nature, rather than of an implicative or logical one. It is fair to say his findings have scientific implications in the sense that they can provide evidence for or imply faults in the scientific model of osteoarthritis. Likewise, in the sense that they imply that – given this is the question we want answered – research should be performed to test whether it is useful to provide treatment targeting cartilage directly. But it does not follow logically from his results that this is what should be done in clinical practice.

Note that it may be the case that from other research it is already known that cartilage is a bad target for treatment, and it may also be known what type of treatment is generally useful to treat cartilage-related pain. In that situation the implication made by the researcher would be an actual implication in the sense that it follows logically from acquired knowledge, but it is based on other research or existing knowledge, rather than on the cross-sectional study. Thus, I argue that the putative implications from cross-sectional studies are either actually speculations (which have value of their own, but should be distinguished from implications), or when they are actual practical implications, they do not follow from the research presented, but rather from knowledge already present. One exception to this may be when cross-sectional studies have negative results. Specifically, when a cross-sectional study falsifies one of the premises underlying some practical application, this could imply that the practice is unsound and should stop being implemented. This illustrates how it is easier to disprove than to prove a hypothesis and thus how falsification leads to greater certainty than verification (Popper, 1963). Ironically though, negative findings are published less often and less quickly than positive findings (Fanelli, 2012; Hopewell, Loudon, Clarke, Oxman, & Dickersin, 2009). I realize this issue of speculation and implication may seem to border on terminological nagging, but I insist there are real consequences to the problem. It is similar to researchers overvaluing single-study results (Ioannidis, 2005, 2007) and analogous to the lack of understanding of statistics in science, which leads researchers to perform 'statistical rituals' rather than statistical analyses, and draw wrong conclusions from their data (Gigerenzer, 2018). I submit that insufficient understanding and improper reporting of practical implications can lead to poor and inefficient science (when researchers do not grasp well enough what their results mean), less trust in science

(when illegitimate claims turn out to be illegitimate in public), and, in the worst case, harmful changes to daily practice (when unfounded recommendations have unforeseen negative effects).

One other complicating factor in drawing practical implications is present not only in cross-sectional studies specifically, but neurobiological research in general. It concerns the translation from (basic) neurobiological function to real-world behavior, outcomes, and treatment. This translation is often more complex than for other types of research (Marincola, 2003). To continue the example of osteoarthritis, it is a fairly simple and direct route from cartilage erosion to knee pain, making it relatively easy to assess where in the mechanism one could intervene. But it is a more complex and less straightforward route from, for example, increased oxygen saturation in particular parts of the brain during a specific moral evaluation lab-setting task to callous-unemotional psychopathic traits (chapter 3), let alone how this translates to a real-world situation such as performing a criminal act. Due to this translation problem, neuroscience has been of limited use in the development of clinically relevant tools (Kapur, Phillips, & Insel, 2012) and has generally not improved treatment (Roiser, 2015). Some researchers have argued the translation problem is largely due to the way neuroscience is being performed. They suggest the methodologies are mainly of a descriptive rather than an explanatory nature and that a different approach is needed (Jonas & Kording, 2017). Others argue larger data sets are necessary to inform more complex models of behavior to bridge the gap between basic neuroscience and clinical practice (Nachev, Rees, & Frackowiak, 2018; Woo, Chang, Lindquist, & Wager, 2017). In any case, the translation problem warrants sincere caution in interpreting what neuroscientific findings mean and could mean for clinical practice.

Scientific implications and future research

Reverting to the current thesis, when we conclude from our cross-sectional research that multi-problem young adults show aberrant early error processing on a neural level compared to healthy controls (chapter 4), it does not logically follow that aberrant error processing itself is something we should start treating in this population to make any progress with regards to their antisocial behavior or societal problems. There exists some evidence that early neural error processing is alterable with specific training, although results of various studies have been mixed (Konicar et al., 2015; Larson et al., 2013; Saunders, Rodrigo, & Inzlicht, 2016; Schoenberg et al., 2013). It may be the case that this is also possible in multi-problem young adults, and that an improvement of neural error processing can lead to better outcome. However, it may also be the case that error processing deficits are untreatable in this population, that if error processing deficits are normalized on a neural level it does not have an

impact on behavior and outcome, or that there are other ways that circumvently solve the same problem in an easier or better manner. For example, in ADHD research a training that robustly improved working memory task performance (Klingberg et al., 2005) did not improve real-world outcomes such as school performance (Redick, Shipstead, Wiemers, Melby-Lervåg, & Hulme, 2015). As with the fictional example of osteoarthritis, rather than having clinical implications, our research leads to new hypotheses that have implications for what kind of scientific study to do next; with the simplest, sensible, and still speculative reasoning being to investigate whether treatment intended to increase error processing can have a positive impact on treatment outcome measures.

To further our understanding of how neurobiological processes function and vary across antisocial populations and behaviors, these processes should be investigated from a more developmental perspective. Large and long-term cohort studies are needed to assess the development of the relationships between antisocial behaviors and neurobiology as these may change over time and vary across developmental phases (see chapters 4 and 5). For example, after entering adulthood resting heart rate does not change with age (Kostis et al., 1982), but the ERN seems to decrease with age (Hoffmann & Falkenstein, 2011), and for the Pe evidence is mixed (Davies et al., 2004; Grammer et al., 2014; Santesso et al., 2006). Taking into account the natural development of these processes may shed light on why findings vary across samples of different ages. In addition, it is relevant to study naturalistic samples, such as multi-problem young adults, as neural correlates of behavior in clinical samples may differ from neural correlates of behavior measured within pertinent samples.

The findings from our longitudinal study (chapter 6) suggest that adding neurobiological measures to risk assessments may be a viable way to improve the predictive accuracy of recidivism. As of yet, too few studies have been performed to justify implementation of this type of risk assessment in practice, but the empirical evidence for such risk assessment is growing. As it likely partly captures a different part of the prediction than known risk factors such as history of delinquency and drug use contain, neurobiological measures have the potential to significantly increase the quality of risk assessment in judicial practice. Such neurobiologically informed assessment may be useful in decision making processes, for example regarding treatment and probation. Importantly, whereas when we try to understand the relationship between neurobiology and antisocial behavior, it is essential that we improve our mechanistic understanding; when we merely use neurobiological measures as tools to predict antisocial behavior, it is initially unnecessary to understand how and why this is the case (Moons, Royston, Vergouwe, Grobbee, & Altman, 2009). Given that our mechanistic understanding of these processes is still limited, I expect this type of predictive modelling to be one of the most rational and effective ways of

implementing neurobiological research for clinical and judicial practice in the short term.

In addition to whether prediction models that include neurobiological measures can perform sufficiently reliable, it is relevant to assess how feasible it is to acquire such data outside laboratory setting and without too high costs. For example, even if an fMRI measure would robustly add to the predictive power of a model for delinquency, its high cost and complex equipment limit its usability in many settings. In contrast, basic ANS measures are fairly easy to acquire, little expertise is needed, and they are very cheap. EEG measures are of intermediate feasibility, requiring more data processing before providing usable variables. Finally, future predictive studies should incorporate basic ANS and EEG measures as these are most feasible and results need to be replicated. Studies should be performed in larger and cross-validated samples to assess robustness of the predictive model, and take place in settings in which actual implementation could take place, such as prisons.

References

References

Achenbach, T. M., & Rescorla, L. A. (2003). Manual for the ASEBA Adult Forms & Profiles. Burlington, VT.

Aghajani, M., Klapwijk, E. T., van der Wee, N. J., Veer, I. M., Rombouts, S. A. R. B., Boon, A. E., … Colins, O. F. (2017). Disorganized Amygdala Networks in Conduct-Disordered Juvenile Offenders With Callous-Unemotional Traits. Biological Psychiatry, 82(4), 283–293. http://doi.org/10.1016/j.biopsych.2016.05.017

Aharoni, E. (2014). Predictive accuracy in the neuroprediction of rearrest, 9(4), 332–336. http://doi.org/10.1016/j.asieco.2008.09.006.EAST

Aharoni, E., Vincent, G. M., Harenski, C. L., Calhoun, V. D., Sinnott-Armstrong, W., Gazzaniga, M. S., & Kiehl, K. a. (2013). Neuroprediction of future rearrest. Proceedings of the National Academy of Sciences of the United States of America, 110(15), 6223–8. http://doi.org/10.1073/pnas.1219302110

Altman, D. G., & Royston, P. (2006). The cost of dichotomising continuous variables. Bmj, 332(7549), 1080.1. http://doi.org/10.1136/bmj.332.7549.1080

Andershed, H., Hodgins, S., & Tengström, A. (2007). Convergent validity of the Youth Psychopathic Traits Inventory (YPI): Association with the Psychopathy Checklist: Youth Version (PCL:YV). Assessment, 14(2), 144–154. http://doi.org/10.1177/1073191106298286

Andrews, D. A., & Bonta, J. (1994). The psychology of criminal conduct. (T. & F. Inc, Ed.).

Arnett, J. J. (2000). Emerging adulthood: A theory of development from the late teens through the twenties. American Psychologist, 55(5), 469–480. Retrieved from http://doi.apa.org/getdoi.cfm?doi=10.1037/0003-066X.55.5.469

Arnett, J. J. (2007). Emerging adulthood: What is it, and what is it good for? Child Development Perspectives, 1(2), 68–73. Retrieved from http://onlinelibrary.wiley.com/doi/10.1111/j.1750-8606.2007.00016.x/full

Arnett, J. J., Žukauskiene, R., & Sugimura, K. (2014). The new life stage of emerging adulthood at ages 18-29 years: Implications for mental health. The Lancet Psychiatry, 1(7), 569–576. http://doi.org/10.1016/S2215-0366(14)00080-7

Baggio, S., Iglesias, K., Deline, S., Studer, J., Henchoz, Y., Mohler-Kuo, M., & Gmel, G. (2015). Not in education, employment, or training status among young Swiss men. Longitudinal associations with mental health and substance use. Journal of Adolescent Health. http://doi.org/10.1016/j.jadohealth.2014.09.006

Beauchaine, T. P., Bell, Z., Knapton, E., McDonough-Caplan, H., Shader, T., & Zisner, A.

(2019). Respiratory sinus arrhythmia reactivity across empirically based structural dimensions of psychopathology: A meta-analysis. Psychophysiology, (June 2018), 1–19. http://doi.org/10.1111/psyp.13329

Beauchaine, T. P., Gatzke-Kopp, L., & Mead, H. K. (2007). Polyvagal Theory and developmental psychopathology: emotion dysregulation and conduct problems from preschool to adolescence. Biological Psychology, 74(2), 174–84. http://doi.org/10.1016/j.biopsycho.2005.08.008

Beauchaine, T. P., Gatzke-Kopp, L., Neuhaus, E., Chipman, J., Reid, M. J., & Webster-Stratton, C. (2013). Sympathetic- and parasympathetic-linked cardiac function and prediction of externalizing behavior, emotion regulation, and prosocial behavior among preschoolers treated for ADHD. Journal of Consulting and Clinical Psychology, 81(3), 481–493. http://doi.org/10.1037/a0032302

Beauchaine, T. P., Hong, J., & Marsh, P. (2008). Sex differences in autonomic correlates of conduct problems and aggression. Journal of the American Academy of Child and Adolescent Psychiatry, 47(7), 788–796. http://doi.org/10.1097/CHI.0b013e318172ef4b

Bennett, C. M., & Miller, M. B. (2010). How reliable are the results from functional magnetic resonance imaging? Annals of the New York Academy of Sciences, 1191, 133–155. http://doi.org/10.1111/j.1749-6632.2010.05446.x

Bernstein, P. S., Scheffers, M. K., & Coles, M. G. H. (1995). "Where did I go wrong?" A psychophysiological analysis of error detection. Journal of Experimental Psychology: Human Perception and Performance, 21(6), 1312–1322. http://doi.org/10.1037/0096-1523.21.6.1312

Berzin, S. C. (2010). Vulnerability in the transition to adulthood: Defining risk based on youth profiles. Children and Youth Services Review, 32(4), 487–495. http://doi.org/10.1016/j.childyouth.2009.11.001

Birbaumer, N., Veit, R., Lotze, M., Erb, M., Hermann, C., Grodd, W., & Flor, H. (2005). Deficient Fear Conditioning in Psychopathy. Archives of General Psychiatry, 62(7), 799–805. http://doi.org/10.1001/archpsyc.62.7.799

Blair, R. (2007). The amygdala and ventromedial prefrontal cortex in morality and psychopathy. Trends in Cognitive Sciences, 11(9), 387–92. http://doi.org/10.1016/j.tics.2007.07.003

Blair, R. (2013). The neurobiology of psychopathic traits in youths. Nature Reviews Neuroscience, 14(11), 786–799. http://doi.org/10.1038/nrn3577.The

Blair, R. (2005). Applying a cognitive neuroscience perspective to the disorder of psychopathy. Development and Psychopathology, 17(3), 865–891. http://doi.org/10.1017/S0954579405050418

Blair, R. (2013). Psychopathy: Cognitive and neural dysfunction. Dialogues in Clinical Neuroscience, 15(2), 181–190. http://doi.org/10.1093/acprof:oso/9780195130157.003.0006

Blyler, C. R., Gold, J. M., Iannone, V. N., & Buchanan, R. W. (2000a). Short form of the WAIS-III for use with patients with schizophrenia. Schizophrenia Research, 46(2–3), 209–15. http://doi.org/10.1016/S0920-9964(00)00017-7

Boonmann, C., Jansen, L. M. C., 'T Hart-Kerkhoffs, L. A., Vahl, P., Hillege, S. L., Doreleijers, T. A. H., & Vermeiren, R. R. J. M. (2015). Self-reported psychopathic traits in sexually offending juveniles compared with generally offending juveniles and general population youth. International Journal of Offender Therapy and Comparative Criminology, 59(1), 85–95. http://doi.org/10.1177/0306624X13508612

Brazil, I. A., De Bruijn, E. R. A., Bulten, B. H., Von Borries, A. K. L., Van Lankveld, J. J. D. M., Buitelaar, J. K., & Verkes, R. J. (2009). Early and late components of error monitoring in violent offenders with psychopathy. Biological Psychiatry, 65(2), 137–143. http://doi.org/10.1016/j.biopsych.2008.08.011

Brazil, I. A., Mars, R. B., Bulten, B. H., Buitelaar, J. K., Verkes, R. J., & De Bruijn, E. R. A. (2011). A neurophysiological dissociation between monitoring one's own and others' actions in psychopathy. Biological Psychiatry, 69(7), 693–699. http://doi.org/10.1016/j.biopsych.2010.11.013

Bresin, K., Sima Finy, M., Sprague, J., & Verona, E. (2014). Response monitoring and adjustment: Differential relations with psychopathic traits. Journal of Abnormal Psychology, 123(3), 634–649. http://doi.org/10.1037/a0037229

Budhani, S., Richell, R. a, & Blair, R. J. R. (2006). Impaired reversal but intact acquisition: probabilistic response reversal deficits in adult individuals with psychopathy. Journal of Abnormal Psychology, 115(3), 552–558. http://doi.org/10.1037/0021-843X.115.3.552

Buuren van, S. (2012). Flexible imputation of missing data. Boca Raton, FL: CRC press.

Bzdok, D., Schilbach, L., Vogeley, K., Schneider, K., Laird, A. R., Langner, R., & Eickhoff, S. B. (2012). Parsing the neural correlates of moral cognition: ALE meta-analysis on morality, theory of mind, and empathy. Brain Structure & Function, 217(4), 783–96. http://doi.org/10.1007/s00429-012-0380-y

Chan, S.-C., Raine, A., & Lee, T. M. C. (2010). Attentional bias towards negative affect stimuli and reactive aggression in male batterers. Psychiatry Research, 176(2–3), 246–9. http://doi.org/10.1016/j.psychres.2008.12.013

Cima, M., Raine, A., Meesters, C., & Popma, A. (2013). Validation of the Dutch Reactive Proactive Questionnaire (RPQ): differential Correlates of Reactive and Proactive Aggression from childhood to adulthood. Aggressive Behavior, 39(2), 99–113. http://doi.org/10.1002/ab.21458

Cima, M., Tonnaer, F., & Hauser, M. D. (2010). Psychopaths know right from wrong but don't care. Social Cognitive and Affective Neuroscience, 5(1), 59–67. http://doi.org/10.1093/scan/

nsp051

Cleckley, H. (1941). The Mask of Sanity. St. Louis, MO: CVMosby.

Coghill, D., & Sonuga-Barke, E. J. S. (2012). Annual research review: Categories versus dimensions in the classification and conceptualisation of child and adolescent mental disorders - Implications of recent empirical study. Journal of Child Psychology and Psychiatry and Allied Disciplines, 53(5), 469–489. http://doi.org/10.1111/j.1469-7610.2011.02511.x

Colins, O. F., & Andershed, H. (2015). The Youth Psychopathic Traits Inventory-Short Version in a General Population Sample of Emerging Adults. Psychological Assessment, 28(5), 449–457. http://doi.org/10.1037/pas0000189

Collins, L. M., Murphy, S. A., & Bierman, K. L. (2004). A conceptual framework for adaptive preventive interventions. Prev Sci, 5(3), 185–196. http://doi.org/10.1023/B:PREV.0000037641.26017.00

Contreras-Rodríguez, O., Pujol, J., Batalla, I., Harrison, B. J., Bosque, J., Ibern-regàs, I., … Cardoner, N. (2014). Disrupted neural processing of emotional faces in psychopathy. Social Cognitive and Affective Neuroscience, 9(4), 505–512. http://doi.org/10.1093/scan/nst014

Cooke, D. J., & Michie, C. (2001). Refining the construct of psychopathy: towards a hierarchical model. Psychological Assessment, 13(2), 171–188. http://doi.org/10.1037/1040-3590.13.2.171

Cornet, L. J. M., De Kogel, C. H., Nijman, H. L. I., Raine, A., & Van Der Laan, P. H. (2014). Neurobiological factors as predictors of cognitive-behavioral therapy outcome in individuals with antisocial behavior: A review of the literature. International Journal of Offender Therapy and Comparative Criminology, 58(11), 1279–1296. http://doi.org/10.1177/0306624X13494694

Cottle, C. C., Lee, R. J., & Heilbrun, K. (2001). The prediction of criminal recidivism in juveniles: A meta-analysis. Criminal Justice and Behavior, 28(3), 367–394. http://doi.org/10.1177/0093854801028003005

Schoenfeld, D. (1982). Partial Residuals for The Proportionnal Hazards Regression Model. Biometrika, 69(1), 239–241. Retrieved from http://www.jstor.org/stable/2335876

Dannlowski, U., Stuhrmann, A., Beutelmann, V., Zwanzger, P., Lenzen, T., Grotegerd, D., … Kugel, H. (2012). Limbic scars: long-term consequences of childhood maltreatment revealed by functional and structural magnetic resonance imaging. Biological Psychiatry, 71(4), 286–93. http://doi.org/10.1016/j.biopsych.2011.10.021

Davies, P. L., Segalowitz, S. J., & Gavin, W. J. (2004). Development of Response-Monitoring ERPs in 7- to 25-Year-Olds. Developmental Neuropsychology, 25(3), 355–376. http://doi.org/10.1207/s15326942dn2503_6

Davis, M., & Stoep, A. (1997). The transition to adulthood for youth who have serious emotional disturbance: Developmental transition and young adult outcomes. The Journal of Behavioral Health Services & Research, 24(4), 400–427. http://doi.org/10.1007/BF02790503

De Wied, M., Boxtel, A. Van, Posthumus, J. a, Goudena, P. P., & Matthys, W. (2009). Facial EMG and heart rate responses to emotion-inducing film clips in boys with disruptive behavior disorders. Psychophysiology, 46(5), 996–1004. http://doi.org/10.1111/j.1469-8986.2009.00851.x

de Wied, M., van Boxtel, A., Matthys, W., & Meeus, W. (2012). Verbal, facial and autonomic responses to empathy-eliciting film clips by disruptive male adolescents with high versus low callous-unemotional traits. Journal of Abnormal Child Psychology, 40(2), 211–23. http://doi.org/10.1007/s10802-011-9557-8

Decety, J., Michalska, K. J., Akitsuki, Y., & Lahey, B. B. (2009). Atypical empathic responses in adolescents with aggressive conduct disorder: a functional MRI investigation. Biological Psychology, 80(2), 203–11. http://doi.org/10.1016/j.biopsycho.2008.09.004

Dehaene, S., & Tucker, D. M. (1994). Technical Commentary LOCALIZATION OF A NEURAL SYSTEM FOR ERROR DETECTION AND COMPENSATION, 5(5), 303–305.

Dembo, R., Wareham, J., Schmeidler, J., & Winters, K. C. (2016). Longitudinal Effects of a Second-Order Multi-Problem Factor of Sexual Risk, Marijuana Use, and Delinquency on Future Arrest Among Truant Youths. Journal of Child and Adolescent Substance Abuse. http://doi.org/10.1080/1067828X.2016.1153554

Dietrich, A., Riese, H., Sondeijker, F. E. P. L., Greaves-Lord, K., van Roon, A. M., Ormel, J., … Rosmalen, J. G. M. (2007). Externalizing and internalizing problems in relation to autonomic function: a population-based study in preadolescents. Journal of the American Academy of Child and Adolescent Psychiatry, 46(3), 378–86. http://doi.org/10.1097/CHI.0b013e31802b91ea

Dikman, Z. V., & Allen, J. J. B. (2000). Error monitoring during reward and avoidance learning in high- and low-socialized individuals. Psychophysiology, 37(1), 43–54. http://doi.org/10.1111/1469-8986.3710043

Dillon, D. G., Holmes, A. J., Birk, J. L., Brooks, N., Lyons-Ruth, K., & Pizzagalli, D. a. (2009). Childhood adversity is associated with left basal ganglia dysfunction during reward anticipation in adulthood. Biological Psychiatry, 66(3), 206–13. http://doi.org/10.1016/j.biopsych.2009.02.019

Dodge, K. A. (1991). The structure and function of reactive and reactive aggression. In D. J. Pepler & K. H. Rubin (Eds.), The development and treatment of childhood aggression (pp. 201–218). Hillsdale, NJ.

Donovan, J. E., & Jessor, R. (1985). Structure of problem behavior in adolescence and young adulthood. Journal of Consulting and Clinical Psychology, 53(6), 890–904. http://doi.org/Cited By (since 1996) 586\rExport Date 21 February 2012

Doreleijers, T. A. H., Moser, F., Thijs, P., Van Engeland, H., & Beyaert, F. H. L. (2000). Forensic assessment of juvenile delinquents: Prevalence of psychopathology and decision-making at court in the Netherlands. Journal of Adolescence, 23(3), 263–275. http://doi.org/10.1006/jado.2000.0313

Duin, L., Bevaart, F., Paalman, C. H., Luijks, M.-J. A., Zijlmans, J., Marhe, R., … Popma, A. (2017). Child Protection Service interference in childhood and the relation with mental health problems and delinquency in young adulthood: A latent class analysis study. Child and Adolescent Psychiatry and Mental Health, 11(1). http://doi.org/10.1186/s13034-017-0205-0

Edens, J. F., Marcus, D. K., Lilienfeld, S. O., & Poythress, N. G. (2006). Psychopathic, not psychopath: taxometric evidence for the dimensional structure of psychopathy. Journal of Abnormal Psychology, 115(1), 131–144. http://doi.org/10.1037/0021-843X.115.1.131

Edwards, B. G., Calhoun, V. D., & Kiehl, K. A. (2012). Joint ICA of ERP and fMRI during error-monitoring. NeuroImage, 59(2), 1896–1903. http://doi.org/10.1016/j.neuroimage.2011.08.088

Eriksen, B. A., & Eriksen, C. W. (1974). Effects of noise letters upon the identification of a target letter in a nonsearch task. Perception & Psychophysics, 16(1), 143–149. http://doi.org/10.3758/BF03203267

Falkenstein, M., Hohnsbein, J., Hoormann, J., & Blanke, L. (1990). Effects of errors in choice reaction tasks on the ERP under focused and divided attention. Psychophysiological Brain Research, 1, 192–195.

Fanelli, D. (2012). Negative results are disappearing from most disciplines and countries. Scientometrics, 90(3), 891–904. http://doi.org/10.1007/s11192-011-0494-7

Fassaert, T., Lauriks, S., Van De Weerd, S., Theunissen, J., Kikkert, M., Dekker, J., … De Wit, M. (2014). Psychometric properties of the Dutch version of the self-sufficiency matrix (SSM-D). Community Mental Health Journal. http://doi.org/10.1007/s10597-013-9683-6

Fergusson, D. M., Boden, J. M., & Horwood, L. J. (2010). Classification of behavior disorders in adolescence: scaling methods, predictive validity, and gender differences. Journal of Abnormal Psychology, 119(4), 699–712. http://doi.org/10.1037/a0018610

Fink, B. C., Tant, A. S., Tremba, K., & Kiehl, K. A. (2012). Assessment of Psychopathic Traits in an Incarcerated Adolescent Sample: A Methodological Comparison. Journal of Abnormal Child Psychology, 40(6), 971–986.

Font, S. A., & Maguire-Jack, K. (2016). Pathways from childhood abuse and other adversities to adult health risks: The role of adult socioeconomic conditions. Child Abuse and Neglect, 51, 390–399. http://doi.org/10.1016/j.chiabu.2015.05.013

Fox, C. L., Towe, S. L., Stephens, R. S., Walker, D. D., & Roffman, R. A. (2011). Motives for

cannabis use in high-risk adolescent users. Psychology of Addictive Behaviors, 25(3), 492–500. http://doi.org/10.1037/a0024331

Frick, P. J., Cornell, A. H., Barry, C. T., Bodin, S. D., & Dane, H. E. (2003). Callous-unemotional traits and conduct problems in the prediction of conduct problem severity, aggression, and self-report of delinquency. Journal of Abnormal Child Psychology, 31(4), 457–70. Retrieved from http://www.ncbi.nlm.nih.gov/pubmed/12831233

Frick, P. J., & White, S. F. (2008). Research review: the importance of callous-unemotional traits for developmental models of aggressive and antisocial behavior. Journal of Child Psychology and Psychiatry, and Allied Disciplines, 49(4), 359–75. http://doi.org/10.1111/j.1469-7610.2007.01862.x

Fumagalli, M., & Priori, A. (2012). Functional and clinical neuroanatomy of morality. Brain, 135(7), 2006–2021. http://doi.org/10.1093/brain/awr334

Garland, A. ., Aarons, G. A., Brown, S. A., Wood, P. A., & Hough, R. L. (2003). Diagnostic Profiles Associated With Use of Mental Health and Substance Abuse Services Among High-Risk Youths. Psychiatric Services, 54(4), 562–564.

Garrigan, B., Adlam, A. L. R., & Langdon, P. E. (2016). The neural correlates of moral decision-making: A systematic review and meta-analysis of moral evaluations and response decision judgements. Brain and Cognition, 108, 88–97. http://doi.org/10.1016/j.bandc.2016.07.007

Gigerenzer, G. (2018). Statistical Rituals: The Replication Delusion and How We Got There. Advances in Methods and Practices in Psychological Science, 1(2), 198–218. http://doi.org/10.1016/S0022-5347(17)50063-4

Gilbert, R., Widom, C. S., Browne, K., Fergusson, D., Webb, E., & Janson, S. (2009). Burden and consequences of child maltreatment in high-income countries. The Lancet, 373(9657), 68–81. http://doi.org/10.1016/S0140-6736(08)61706-7

Glenn, A. L., Raine, A., & Schug, R. A. (2009). The neural correlates of moral decision-making in psychopathy. Molecular Psychiatry, 14(1), 5–6. http://doi.org/10.1038/mp.2008.83

Glenn, A. L., Raine, A., Schug, R. A., Young, L., & Hauser, M. (2009). Increased DLPFC activity during moral decision-making in psychopathy. Molecular Psychiatry, 14(10), 909–911. http://doi.org/10.1038/mp.2009.76

Grammer, J. K., Carrasco, M., Gehring, W. J., & Morrison, F. J. (2014). Age-related Changes in Error Processing in Young Children: A School-based Investigation. Developmental Cognitive Neuroscience, 9, 93–105. http://doi.org/10.1016/j.dcn.2014.02.001

Gratton, G., Coles, M. G. H., & Donchin, E. (1983). A new method for off-line removal of ocular artifact. Electroencephalography and Clinical Neurophysiology, 55, 468–484.

Graziano, P., & Derefinko, K. (2013). Cardiac vagal control and children's adaptive functioning: A meta-analysis. Biological Psychology, 94(1), 22–37. http://doi.org/10.1016/j.biopsycho.2013.04.011

Greene, J. D., Sommerville, R. B., Nystrom, L. E., Darley, J. M., & Cohen, J. D. (2001). An fMRI investigation of emotional engagement in moral judgment. Science, 293(5537), 2105–8. http://doi.org/10.1126/science.1062872

Gross, J., & Levenson, R. (1995). Emotion elicitation using films. Cognition & Emotion, 9(1), 87–108. Retrieved from http://www.tandfonline.com/doi/abs/10.1080/02699939508408966

Grossman, P., & Taylor, E. W. (2007). Toward understanding respiratory sinus arrhythmia: Relations to cardiac vagal tone, evolution and biobehavioral functions. Biological Psychology, 74(2), 263–285. http://doi.org/10.1016/j.biopsycho.2005.11.014

Guay, J.-P., Ruscio, J., Knight, R. a, & Hare, R. D. (2007). A Taxometric Analysis of the Latent Structure of Psychopathy: Evidence for Dimensionality. Journal of Abnormal Psychology, 116(4), 701–716. http://doi.org/10.1037/0021-843X.116.4.701

Hajcak, G., Moser, J. S., Yeung, N., & Simons, R. F. (2005). On the ERN and the significance of errors. Psychophysiology, 42(2), 151–60. http://doi.org/10.1111/j.1469-8986.2005.00270.x

Hall, J. R., Bernat, E. M., & Patrick, C. J. (2007). Externalizing psychopathology and the error-related negativity. Psychological Science, 18(4), 326–333. http://doi.org/10.1111/j.1467-9280.2007.01899.x

Hare, R. D. (2003). The Hare Psychopathy Checklist—Revised. Toronto, Ontario, Canada: Multi-Health Systems.

Hare, R. D., & Neumann, C. S. (2008). Psychopathy as a Clinical and Empirical Construct. Annual Review of Clinical Psychology, 4(1), 217–246. http://doi.org/10.1146/annurev.clinpsy.3.022806.091452

Harenski, C. L., Edwards, B. G., Harenski, K. A., & Kiehl, K. A. (2014a). Neural correlates of moral and non-moral emotion in female psychopathy. Frontiers in Human Neuroscience, 8, 1–10. http://doi.org/10.3389/fnhum.2014.00741

Harenski, C. L., & Hamann, S. (2006). Neural correlates of regulating negative emotions related to moral violations. NeuroImage, 30(1), 313–24. http://doi.org/10.1016/j.neuroimage.2005.09.034

Harenski, C. L., Harenski, K. A., & Kiehl, K. A. (2014b). Neural processing of moral violations among incarcerated adolescents with psychopathic traits. Developmental Cognitive Neuroscience, 10, 181–189. http://doi.org/10.1016/j.dcn.2014.09.002

Harenski, C. L., Harenski, K. A., Shane, M. S., & Kiehl, K. A. (2010). Aberrant neural

processing of moral violations in criminal psychopaths. Journal of Abnormal Psychology, 119(4), 863–74. http://doi.org/10.1037/a0020979

Hart, H., & Rubia, K. (2012). Neuroimaging of child abuse: a critical review. Frontiers in Human Neuroscience, 6(March), 52. http://doi.org/10.3389/fnhum.2012.00052

Hawkins, E. H. (2009). A Tale of Two Systems: Co-Occurring Mental Health and Substance Abuse Disorders Treatment for Adolescents. Annual Review of Psychology. http://doi.org/10.1146/annurev.psych.60.110707.163456

Heagerty, P. J., & Zheng, Y. (2005). Survival model predictive accuracy and ROC curves 1. Biometrics, 61(0006–341X (Print)), 92–105. http://doi.org/10.1111/j.0006-341X.2005.030814.x

Heekeren, H. R., Wartenburger, I., Schmidt, H., Schwintowski, H.-P., & Villringer, A. (2003). An fMRI study of simple ethical decision-making. Neuroreport, 14(9), 1215–1219. http://doi.org/10.1097/01.wnr.0000081878.45938.a7

Henry, K. L., Knight, K. E., & Thornberry, T. P. (2012). School Disengagement as a Predictor of Dropout, Delinquency, and Problem Substance Use During Adolescence and Early Adulthood. Journal of Youth and Adolescence. http://doi.org/10.1007/s10964-011-9665-3

Heritage, A. J., & Benning, S. D. (2013). Impulsivity and response modulation deficits in psychopathy: Evidence from the ERN and N1. Journal of Abnormal Psychology, 122(1), 215–222. http://doi.org/10.1037/a0030039

Herpertz, S. C., Wenning, B., Mueller, B., Qunaibi, M., Sass, H., & Herpertz-Dahlmann, B. (2001). Psychophysiological responses in ADHD boys with and without conduct disorder: Implications for adult antisocial behavior. Journal of the American Academy of Child and Adolescent Psychiatry, 40(10), 1222–1230. http://doi.org/10.1097/00004583-200110000-00017

Hill, J. M., Blokland, A. A. J., & Van Der Geest, V. R. (2018). Risk factors for self-reported delinquency in emerging adulthood. European Journal of Criminology, 1–23. http://doi.org/10.1177/1477370817749495

Hoffmann, S., & Falkenstein, M. (2011). Aging and error processing: Age related increase in the variability of the error-negativity is not accompanied by increase in response variability. PLoS ONE, 6(2). http://doi.org/10.1371/journal.pone.0017482

Holroyd, C. B., & Coles, M. G. H. (2002). The neural basis. of human error processing: Reinforcement learning, dopamine, and the error-related negativity. Psychological Review, 109(4), 679–709. http://doi.org/10.1037//0033-295X.109.4.679

Hopewell, S., Loudon, K., Clarke, M. J., Oxman, A. D., & Dickersin, K. (2009). Publication bias in clinical trials due to statistical significance or direction of trial results. Cochrane Database of Systematic Reviews, (1). http://doi.org/10.1002/14651858.MR000006.pub3

Hosmer, D., & Lemeshow, S. (2000). Applied Logistic Regression (Second edi). New York, NY: John Wiley & Sons.

Hoyle, R. H., Stephenson, M. T., Palmgreen, P., Lorch, E. P., & Donohew, R. L. (2002). Reliability and validity of a brief measure of sensation seeking. Personality and Individual Differences, 32(3), 401–414. http://doi.org/10.1016/S0191-8869(01)00032-0

Hyde, L. W., Shaw, D. S., & Hariri, A. R. (2013). Understanding youth antisocial behavior using neuroscience through a developmental psychopathology lens: Review, integration, and directions for research. Developmental Review, 33(3), 168–223. http://doi.org/10.1016/j.dr.2013.06.001

Ioannidis, J. P. A. (2005). Why most published research findings are false. PLoS Medicine, 2(8), e124. http://doi.org/10.1371/journal.pmed.0020124

Ioannidis, J. P. A. (2007). Evolution and Translation of Research Findings: From Bench to Where. PLoS Clinical Trials, 2(2), e3. http://doi.org/10.1371/journal.pctr.0020003

Jessor, R. (1992). Risk behavior in adolescence: A psychosocial framework for understanding and action. Journal of Adolescent Health, 12(8), 597–605. http://doi.org/https://doi.org/10.1016/1054-139X(91)90007-K

Jonas, E., & Kording, K. P. (2017). Could a Neuroscientist Understand a Microprocessor? PLoS Computational Biology, 13(1), 1–24. http://doi.org/10.1371/journal.pcbi.1005268

Kalmakis, K. A., & Chandler, G. E. (2015). Health consequences of adverse childhood experiences: A systematic review. Journal of the American Association of Nurse Practitioners, 27(8), 457–465. http://doi.org/10.1002/2327-6924.12215

Kapur, S., Phillips, A. G., & Insel, T. R. (2012). Why has it taken so long for biological psychiatry to develop clinical tests and what to do about it. Molecular Psychiatry, 17(12), 1174–1179. http://doi.org/10.1038/mp.2012.105

Kiehl, K. A., & Hoffman, M. B. (2011). The criminal psychopathy: history, neuroscience, treatment, and economics. Jurimetrics, 51, 355–397.

Kiehl, K. a. (2006). A cognitive neuroscience perspective on psychopathy: evidence for paralimbic system dysfunction. Psychiatry Research, 142(2–3), 107–28. http://doi.org/10.1016/j.psychres.2005.09.013

Kiehl, K. a, Smith, a M., Hare, R. D., Mendrek, A., Forster, B. B., Brink, J., & Liddle, P. F. (2001). Limbic abnormalities in affective processing by criminal psychopaths as revealed by functional magnetic resonance imaging. Biological Psychiatry, 50(9), 677–84.

Klaver, C., De Geus, E., & De Vries, J. (1994). Ambulatory monitoring system. In F. J. Maarsse, A. E. Akkerman, A. N. Brand, & L. J. M. van der Stelt Mulder (Eds.), Computers in Psychology;

applications, methods, and instrumentation (pp. 254–268). Amsterdam: Swets & Zeitlinger.

Klingberg, T., Fernell, E., Olesen, P. J., Johnson, M., Gustafsson, P., Dahlström, K., … Westerberg, H. (2005). Computerized training of working memory in children with ADHD - A randomized, controlled trial. Journal of the American Academy of Child and Adolescent Psychiatry, 44(2), 177–186. http://doi.org/10.1097/00004583-200502000-00010

Koenigs, M. (2012). The role of prefrontal cortex in psychopathy. Reviews in Neuroscience, 23(3), 253–262. http://doi.org/10.1515/revneuro-2012-0036.The

Konicar, L., Veit, R., Eisenbarth, H., Barth, B., Tonin, P., Strehl, U., & Birbaumer, N. (2015). Brain self-regulation in criminal psychopaths. Scientific Reports, 5(1), 9426. http://doi.org/10.1038/srep09426

Kostis, J. B., Moreyra, A. E., Amendo, M. T., Di Pietro, J., Cosgrove, N., & Kuo, P. T. (1982). The effect of age on heart rate in subjects free of heart disease. Studies by ambulatory electrocardiography and maximal exercise stress test. Circulation, 65(1), 141–145. http://doi.org/10.1161/01.cir.65.1.141

Kreibig, S. D. (2010). Autonomic nervous system activity in emotion: A review. Biological Psychology, 84(3), 394–421. http://doi.org/10.1016/j.biopsycho.2010.03.010

Krueger, R. F., & Markon, K. E. (2013). A Dimensional-Spectrum Model of Psychopathology. Archives of General Psychiatry, 68(1), 10–11. http://doi.org/10.1017/S0033291710001662.5.

Lane, J. A., Leibert, T. W., & Goka-Dubose, E. (2017). The Impact of Life Transition on Emerging Adult Attachment, Social Support, and Well-Being: A Multiple-Group Comparison. Journal of Counseling and Development, 95(4), 378–388. http://doi.org/10.1002/jcad.12153

Lang, P. J., Bradley, M. M., & Cuthbert, B. N. (2008). International Affective Picture System (IAPS): Affective ratings of pictures and instruction manual (Technical Report No. A-8). Gainesville, FL: University of Florida, Center for Research in Psychophysiology.

Larson, M. J., Steffen, P. R., & Primosch, M. (2013). The impact of a brief mindfulness meditation intervention on cognitive control and error-related performance monitoring. Frontiers in Human Neuroscience, 7, 1–12. http://doi.org/10.3389/fnhum.2013.00308

Latvala, A., Kuja-Halkola, R., Almqvist, C., Larsson, H., & Lichtenstein, P. (2015). A longitudinal study of resting heart rate and violent criminality in more than 700000 men. JAMA Psychiatry, 72(10), 971–978. http://doi.org/10.1001/jamapsychiatry.2015.1165

Lauriks, S., de Wit, M. A. S., Buster, M. C. A., Fassaert, T. J. L., van Wifferen, R., & Klazinga, N. S. (2014). The Use of the Dutch Self-Sufficiency Matrix (SSM-D) to Inform Allocation Decisions to Public Mental Health Care for Homeless People. Community Mental Health Journal. http://doi.org/10.1007/s10597-014-9707-x

Lee, T., Festinger, T., Jaccard, J., & Munson, M. R. (2017). Mental Health Subgroups Among Vulnerable Emerging Adults, and Their Functioning. Journal of the Society for Social Work and Research. http://doi.org/10.1086/692019

Lipsey, M. (2007). Effects of cognitive-behavioral programs for criminal offenders. Campbell Systematic Reviews, 6, 1–27. http://doi.org/10.4073/csr.2007.6

Liu, Y., Croft, J. B., Chapman, D. P., Perry, G. S., Greenlund, K. J., Zhao, G., & Edwards, V. J. (2013). Relationship between adverse childhood experiences and unemployment among adults from five US states. Social Psychiatry and Psychiatric Epidemiology, 48(3), 357–369. http://doi.org/10.1007/s00127-012-0554-1

Loeber, R., Farrington, D., & Petechuk, D. (2013). Bulletin 1: From Juvenile Delinquency to Young Adult Offending.

Lorber, M. F. (2004). Psychophysiology of aggression, psychopathy, and conduct problems: a meta-analysis. Psychological Bulletin, 130(4), 531–52. http://doi.org/10.1037/0033-2909.130.4.531

Luck, S. (2014). An introduction to the event-related potential technique (Second edi). Cambridge, MA: The MIT Press.

Luijks, M. J. A., Bevaart, F., Zijlmans, J., Duin, L. van, Marhe, R., Doreleijers, T. A. H., … Popma, A. (2017). A multimodal day treatment program for multi-problem young adults: Study protocol of a randomized controlled trial. Trials, 18(225), 1–15. http://doi.org/10.1186/s13063-017-1950-3

Luijten, M., Veltman, D. J., Hester, R., Smits, M., Nijs, I. M. T., Pepplinkhuizen, L., & Franken, I. H. A. (2013). The role of dopamine in inhibitory control in smokers and non-smokers: A pharmacological fMRI study. European Neuropsychopharmacology, 23(10), 1247–1256. http://doi.org/10.1016/j.euroneuro.2012.10.017

MacKenzie, D. L., & Farrington, D. P. (2015). Preventing future offending of delinquents and offenders: what have we learned from experiments and meta-analyses? Journal of Experimental Criminology, 11(4), 565–595. http://doi.org/10.1007/s11292-015-9244-9

Marhe, R., van de Wetering, B. J. M., & Franken, I. H. A. (2013). Error-related brain activity predicts cocaine use after treatment at 3-month follow-up. Biological Psychiatry, 73(8), 782–788. http://doi.org/10.1016/j.biopsych.2012.12.016

Marincola, F. M. (2003). Translational Medicine : A two-way road, 2, 1–2.

Marlatt, G. A., & Gordon, J. R. (Eds.). (2005). Relapse prevention. New York: Guilford Press.

Marsh, A. a, Finger, E. C., Fowler, K. a, Adalio, C. J., Jurkowitz, I. T. N., Schechter, J. C., … Blair, R. J. R. (2013). Empathic responsiveness in amygdala and anterior cingulate cortex

in youths with psychopathic traits. Journal of Child Psychology and Psychiatry, and Allied Disciplines, 54(8), 900–10. http://doi.org/10.1111/jcpp.12063

Marsh, P., Beauchaine, T. P., & Williams, B. (2008). Dissociation of sad facial expressions and autonomic nervous system responding in boys with disruptive behavior disorders. Psychophysiology, 45(1), 100–10. http://doi.org/10.1111/j.1469-8986.2007.00603.x

Maurer, J. M., Steele, V. R., Cope, L. M., Vincent, G. M., Stephen, J. M., Calhoun, V. D., & Kiehl, K. A. (2015). Dysfunctional error-related processing in incarcerated youth with elevated psychopathic traits. Developmental Cognitive Neuroscience, 57(6), 742–768. http://doi.org/10.1002/dev.21214.Developmental

Maurer, J. M., Steele, V. R., Fink, B. C., Vincent, G. M., Calhoun, V. D., & Kiehl, K. A. (2018). Investigating error-related processing in incarcerated adolescents with self-report psychopathy measures. Biological Psychology, 132(June 2017), 96–105. http://doi.org/10.1016/j.biopsycho.2017.11.009

Maurer, M., Steele, V. R., Edwards, B. G., Bernat, E. M., Calhoun, V. D., & Kiehl, K. A. (2016). Dysfunctional error-related processing in female psychopathy. Social Cognitive and Affective Neuroscience, 11(7), 1059–1068. http://doi.org/10.1093/scan/nsv070

McCollister, K. E., French, M. T., & Fang, H. (2011). The Cost of Crime to Society: New Crime-Specific Estimates for Policy and Program Evaluation. Drug Alcohol Depend, 108, 98–109. http://doi.org/10.1016/j.drugalcdep.2009.12.002.The

McCrory, E. J., De Brito, S. a, Kelly, P. a, Bird, G., Sebastian, C. L., Mechelli, A., … Viding, E. (2013). Amygdala activation in maltreated children during pre-attentive emotional processing. The British Journal of Psychiatry : The Journal of Mental Science, 202(4), 269–76. http://doi.org/10.1192/bjp.bp.112.116624

McParland, D., & Gormley, I. C. (2016). Model based clustering for mixed data: clustMD. Advances in Data Analysis and Classification, 10(2), 155–169. http://doi.org/10.1007/s11634-016-0238-x

McPherson, K. E., Kerr, S., McGee, E., Morgan, A., Cheater, F. M., McLean, J., & Egan, J. (2014). The association between social capital and mental health and behavioural problems in children and adolescents: an integrative systematic review. BMC Psychology, 2(1), 7. http://doi.org/10.1186/2050-7283-2-7

Meeus, W., & Koot, H. (2007). Codeboek van het onderzoeksproject RADAR. Utrecht en Amsterdam.

Merk, W., Orobio de Castro, B., Koops, W., & Matthys, W. (2005). The distinction between reactive and proactive aggression: Utility for theory, diagnosis and treatment? European Journal of Developmental Psychology, 2(2), 197–220. http://doi.org/10.1080/17405620444000300

Miller, G. E., Chen, E., & Parker, K. J. (2011). Psychological Stress in Childhood and Susceptibility to the Chronic Diseases of Aging: Moving Toward a Model of Behavioral and Biological Mechanisms. Psychological Bulletin. http://doi.org/10.1037/a0024768

Miltenburg, E., Lindo, F., Tzaninis, Y., & Duin, L. Van. (2011). City Survey Report Rotterdam.

Moll, J., de Oliveira-Souza, R., Eslinger, P. J., Bramati, I. E., Mourão-Miranda, J., Andreiuolo, P. A., & Pessoa, L. (2002). The neural correlates of moral sensitivity: a functional magnetic resonance imaging investigation of basic and moral emotions. The Journal of Neuroscience, 22(7), 2730–6. http://doi.org/20026214

Monroe, S. M., & Simons, A. D. (1991). Diathesis stress theories in the context of life stress research - implications for the depressive-disorders. Psychological Bulletin, 110(3), 406–425. http://doi.org/10.1037//0033-2909.110.3.406

Moons, K. G. M., Royston, P., Vergouwe, Y., Grobbee, D. E., & Altman, D. G. (2009). Prognosis and prognostic research: What, why, and how? BMJ (Online), 338(7706), 1317–1320. http://doi.org/10.1136/bmj.b375

Mulder, E., Vermunt, J., Brand, E., Bullens, R., & Marle, H. (2012). Recidivism in subgroups of serious juvenile offenders. Criminal Behaviour and Mental Health, 22(2).

Mun, E. Y., Windle, M., & Schainker, L. M. (2008). A model-based cluster analysis approach to adolescent problem behaviors and young adult outcomes. Development and Psychopathology. http://doi.org/10.1017/S095457940800014X

Munro, G. E. S., Dywan, J., Harris, G. T., McKee, S., Unsal, A., & Segalowitz, S. J. (2007). ERN varies with degree of psychopathy in an emotion discrimination task. Biological Psychology, 76(1–2), 31–42. http://doi.org/10.1016/j.biopsycho.2007.05.004

Murray, J., Hallal, P. C., Mielke, G. I., Raine, A., Wehrmeister, F. C., Anselmi, L., & Barros, F. C. (2016). Low resting heart rate is associated with violence in late adolescence: A prospective birth cohort study in Brazil. International Journal of Epidemiology, 45(2), 491–500. http://doi.org/10.1093/ije/dyv340

Murrie, D. C., Marcus, D. K., Douglas, K. S., Lee, Z., Salekin, R. T., & Vincent, G. (2007). Youth with psychopathy features are not a discrete class: A taxometric analysis. Journal of Child Psychology and Psychiatry and Allied Disciplines, 48(7), 714–723. http://doi.org/10.1111/j.1469-7610.2007.01734.x

Nachev, P., Rees, G., & Frackowiak, R. (2018). Lost in translation. F1000Research, (7), 1–15.

Newman, D. L., Moffitt, T. E., Caspi, A., Magdol, L., Silva, P. A., & Stanton, W. R. (1996). Psychiatric disorder in a birth cohort of young adults: Prevalence, comorbidity, clinical significance, and new case incidence from ages 11 to 21. Journal of Consulting and Clinical

Psychology, 64(3), 552–562. http://doi.org/10.1037/0022-006X.64.3.552

Newman, J. P., & Kosson, D. S. (1986). Passive avoidance learning in psychopathic and nonpsychopathic offenders. Journal of Abnormal Psychology, 95(3), 252–256. http://doi.org/10.1037/0021-843X.95.3.252

Odgers, C. L., Caspi, A., Broadbent, J. M., Dickson, N., Hancox, R. J., Harrington, H., … Moffitt, T. E. (2007). Prediction of differential adult health burden by conduct problem subtypes in males. Archives of General Psychiatry, 64(4), 476–484. http://doi.org/10.1001/archpsyc.64.4.476

Ogilvie, J. M., Stewart, A. L., Chan, R. C. K., & Shum, D. H. K. (2011). Neuropsychological Measures of Executive Function and Antisocial Behavior: a Meta-Analysis*. Criminology, 49(4), 1063–1107. http://doi.org/10.1111/j.1745-9125.2011.00252.x

Oldenhof, H., Prätzlich, M., Ackermann, K., Baker, R., Batchelor, M., Baumann, S., … Popma, A. (2018). Baseline autonomic nervous system activity in female children and adolescents with conduct disorder: Psychophysiological findings from the FemNAT-CD study. Journal of Criminal Justice, (May), 0–1. http://doi.org/10.1016/j.jcrimjus.2018.05.011

Olvet, D. M., & Hajcak, G. (2009). The stability of error-related brain activity with increasing trials. Psychophysiology, 46(5), 957–961. http://doi.org/10.1111/j.1469-8986.2009.00848.x

Ortiz, J., & Raine, A. (2004). Heart Rate Level and Antisocial Behavior in Children and Adolescents : A Meta-Analysis. Journal of the American Academy of Child & Adolescent Psychiatry, 43(2), 154–162. http://doi.org/10.1097/01.chi.0000101373.03068.5c

Osgood, D. W., Foster, E. M., & Courtney, M. E. (2010a). Vulnerable populations and the transition to adulthood. The Future of Children, 20(1), 209–229. http://doi.org/10.1353/foc.0.0047

Osumi, T., Nakao, T., Kasuya, Y., Shinoda, J., Yamada, J., & Ohira, H. (2012). Amygdala dysfunction attenuates frustration-induced aggression in psychopathic individuals in a non-criminal population. Journal of Affective Disorders, 142(1–3), 331–8. http://doi.org/10.1016/j.jad.2012.05.012

Paolacci, G., Chandler, J., & Ipeirotis, P. (2010). Running experiments on amazon mechanical turk. Judgment and Decision Making, 5(5), 411–419. http://doi.org/10.2139/ssrn.1626226

Pasion, R., Cruz, A. R., & Barbosa, F. (2016). Dissociation of boldness and disinhibition psychopathic traits in ERN modulation. Personality and Individual Differences, 95, 6–10. http://doi.org/10.1016/j.paid.2016.02.017

Passamonti, L., Fairchild, G., Goodyer, I. M., Hurford, G., Hagan, C. C., Rowe, J. B., & Calder, A. J. (2010). Neural abnormalities in early-onset and adolescence-onset conduct disorder. Archives

of General Psychiatry, 67(7), 729–738. http://doi.org/10.1001/archgenpsychiatry.2010.75

Patton, J. H., Stanford, M. S., & Barratt, E. S. (1995). Factor structure of the Barratt Impulsiveness Scale. Journal of Clinical Psychology, 51(6), 768–774.

Perkins, K. L. (2017). Reconsidering residential mobility: Differential effects on child wellbeing by race and ethnicity. Social Science Research, 63, 124–137. http://doi.org/10.1016/j.ssresearch.2016.09.024

Piferi, R. L., Kline, K. A., Younger, J., & Lawler, K. A. (2000). An alternative approach for achieving cardiovascular baseline: viewing an aquatic video. International Journal of Psychophysiology, 37(2), 207–217. http://doi.org/10.1016/S0167-8760(00)00102-1

Poldrack, R. A., Monahan, J., Imrey, P. B., Reyna, V., Raichle, M. E., Faigman, D., & Buckholtz, J. W. (2018). Predicting Violent Behavior: What Can Neuroscience Add? Trends in Cognitive Sciences, 22(2), 111–123. http://doi.org/10.1016/j.tics.2017.11.003

Popma, A., & Raine, A. (2006). Will future forensic assessment be neurobiologic? Child and Adolescent Psychiatric Clinics of North America, 15(2), 429–444. http://doi.org/10.1016/j.chc.2005.11.004

Popper, K. (1963). Conjectures and refutations. Routledge & Kegan Paul.

Portnoy, J., & Farrington, D. P. (2015). Resting heart rate and antisocial behavior: An updated systematic review and meta-analysis. Aggression and Violent Behavior, 22, 33–45. http://doi.org/10.1016/j.avb.2015.02.004

Potter, C. C., & Jenson, J. M. (2003). Cluster profiles of multiple problem youth: Mental health problem symptoms, substance use, and delinquent conduct. Criminal Justice and Behavior. http://doi.org/10.1177/0093854802251007

Prätzlich, M., Oldenhof, H., Steppan, M., Ackermann, K., Baker, R., Batchelor, M., … Stadler, C. (2018). Resting autonomic nervous system activity is unrelated to antisocial behaviour dimensions in adolescents_ Cross-sectional findings from a European multi-centre study. Journal of Criminal Justice, (January), 0–1. http://doi.org/10.1016/j.jcrimjus.2018.01.004

Prehn, K., Wartenburger, I., Mériau, K., Scheibe, C., Goodenough, O. R., Villringer, A., … Heekeren, H. R. (2008). Individual differences in moral judgment competence influence neural correlates of socio-normative judgments. Social Cognitive and Affective Neuroscience, 3(1), 33–46. http://doi.org/10.1093/scan/nsm037

Priebe, S., Huxley, P., Knight, S., & Evans, S. (1999). Application and results of the Manchester Short Assessment of Quality of Life (MANSA). The International Journal of Social Psychiatry, 45(1), 7–12. Retrieved from http://www.ncbi.nlm.nih.gov/pubmed/10443245

Raine, A. (1993). The Psychopathology of Crime. San Diego, CA: Academic Press.

Raine, A., Dodge, K., Loeber, R., Gatzke-kopp, L., Lynam, D., Reynolds, C., … Liu, J. (2006). The Reactive–Proactive Aggression Questionnaire: Differential Correlates of Reactive and Proactive Aggression in Adolescent Boys. Aggressive Behavior, 32(2), 159–171. http://doi.org/10.1002/ab.20115

Raine, A., Venables, P. H., & Mednick, S. A. (1997). Low resting heart rate at age 3 years predisposes to aggression at age 11 years: evidence from the Mauritius Child Health Project. Journal of the American Academy of Child and Adolescent Psychiatry, 36(10), 1457–1464. http://doi.org/10.1097/00004583-199710000-00029

Raine, A., Venables, P. H., & Williams, M. (1995). High Autonomic Arousal and Electrodermal Orienting at Age 15 Years as Protective Factors Against Criminal Behavior at Age 29 Years. American Journal of Psychiatry, 152(11), 1595–1600.

Rebbe, R., Nurius, P. S., Ahrens, K. R., & Courtney, M. E. (2017). Adverse childhood experiences among youth aging out of foster care: A latent class analysis. Children and Youth Services Review. http://doi.org/10.1016/j.childyouth.2017.02.004

Redick, T. S., Shipstead, Z., Wiemers, E. A., Melby-Lervåg, M., & Hulme, C. (2015). What's Working in Working Memory Training? An Educational Perspective. Educational Psychology Review, 27(4), 617–633. http://doi.org/10.1007/s10648-015-9314-6

Ridderinkhof, K., Ullsperger, M., & Crone, E. (2004). The role of the medial frontal cortex in cognitive control. Science, 443(2004), 443–448. http://doi.org/10.1126/science.1100301

Rilling, J. K., Glenn, A. L., Jairam, M. R., Pagnoni, G., Goldsmith, D. R., Elfenbein, H. a, & Lilienfeld, S. O. (2007). Neural correlates of social cooperation and non-cooperation as a function of psychopathy. Biological Psychiatry, 61(11), 1260–71. http://doi.org/10.1016/j.biopsych.2006.07.021

Roiser, J. P. (2015). What has neuroscience ever done for us? Psychologist, 28, 284–287.

Rosseel, Y. (2012). lavaan: An R Package for Structural Equation Modeling. Journal of Statistical Software, 48(2), 1–36.

Rothman, K. J., Greenland, S., & Lash, T. L. (2012). Modern Epidemiology. (L. W. A. Wilkins, Ed.).

Santesso, D. L., Segalowitz, S. J., & Schmidt, L. A. (2006). Error-related electrocortical responses in 10-year-old children and young adults. Developmental Science, 9(5), 473–481. http://doi.org/10.1111/j.1467-7687.2006.00514.x

Saunders, B., Rodrigo, A. H., & Inzlicht, M. (2016). Mindful awareness of feelings increases neural performance monitoring. Cognitive, Affective and Behavioral Neuroscience, 16(1), 93–105. http://doi.org/10.3758/s13415-015-0375-2

Scarpa, A., Haden, S. C., & Tanaka, A. (2010). Being hot-tempered: Autonomic, emotional, and behavioral distinctions between childhood reactive and proactive aggression. Biological Psychology, 84(3), 488–496. http://doi.org/10.1016/j.biopsycho.2009.11.006

Schippers, G. M., Broekman, T. G., Buchholz, A., Koeter, M. W. J., & van den Brink, W. (2010). Measurements in the Addictions for Triage and Evaluation (MATE): an instrument based on the World Health Organization family of international classifications. Addiction, 105(5), 862–71. http://doi.org/10.1111/j.1360-0443.2009.02889.x

Schoenberg, P. L. A., Kan, C. C., Speckens, A. E. M., Buitelaar, J. K., Barendregt, H. P., & Hepark, S. (2013). Effects of mindfulness-based cognitive therapy on neurophysiological correlates of performance monitoring in adult attention-deficit/hyperactivity disorder. Clinical Neurophysiology, 125(7), 1407–1416. http://doi.org/10.1016/j.clinph.2013.11.031

Schulreich, S. (2016). Altered Performance Monitoring in Psychopathy: A Review of Studies on Action Selection, Error, and Feedback Processing. Current Behavioral Neuroscience Reports, 3(1), 19–27. http://doi.org/10.1007/s40473-016-0061-x

Sebastian, C. L., McCrory, E. J. P., Cecil, C. a M., Lockwood, P. L., De Brito, S. a, Fontaine, N. M. G., & Viding, E. (2012). Neural responses to affective and cognitive theory of mind in children with conduct problems and varying levels of callous-unemotional traits. Archives of General Psychiatry, 69(8), 814–22. http://doi.org/10.1001/archgenpsychiatry.2011.2070

Sevinc, G., & Nathan Spreng, R. (2014). Contextual and perceptual brain processes underlying moral cognition: A quantitative meta-analysis of moral reasoning and moral emotions. PLoS ONE, 9(2). http://doi.org/10.1371/journal.pone.0087427

Sheehan, D. V, Lecrubier, Y., Harnett Sheehan, K., Janavs, J., Weiller, E., Keskiner, A., … Dunbar, G. C. (1997). The validity of the Mini International Neuropsychiatric Interview (MINI) according to the SCID-P and its reliability. European Psychiatry, 12(5), 232–241. http://doi.org/10.1016/S0924-9338(97)83297-X

Shonkoff, J. P., Garner, A. S., Siegel, B. S., Dobbins, M. I., Earls, M. F., Garner, A. S., … Wood, D. L. (2012). The Lifelong Effects of Early Childhood Adversity and Toxic Stress. PEDIATRICS. http://doi.org/10.1542/peds.2011-2663

Singer, M., Bulled, N., Ostrach, B., & Mendenhall, E. (2017). Syndemics and the biosocial conception of health. The Lancet. http://doi.org/10.1016/S0140-6736(17)30003-X

Steele, V. R., Claus, E. D., Aharoni, E., Vincent, G. M., Calhoun, V. D., & Kiehl, K. A. (2015). Multimodal imaging measures predict rearrest. Frontiers in Human Neuroscience, 9(August), 1–13. http://doi.org/10.3389/fnhum.2015.00425

Steele, V. R., Maurer, J. M., Bernat, E. M., Calhoun, V. D., & Kiehl, K. A. (2015). Error-Related Processing in Adult Males with Elevated Psychopathic Traits. Personality Disorders, 20(10), 1878–

1891. http://doi.org/10.1162/jocn.2008.20125.Left-lateralized

Stroud, C., Walker, L. R., Davis, M., & Irwin, C. E. (2015). Investing in the health and well-being of young adults. Journal of Adolescent Health. http://doi.org/10.1016/j.jadohealth.2014.11.012

Tanner, J. L., Reinherz, H. Z., Beardslee, W. R., Fitzmaurice, G. M., Leis, J. A., & Berger, S. R. (2007). Change in prevalence of psychiatric disorders from ages 21 to 30 in a community sample. The Journal of Nervous and Mental Disease, 195(4), 298–306. http://doi.org/10.1097/01.nmd.0000261952.13887.6e

Tassy, S., Deruelle, C., Mancini, J., Leistedt, S., & Wicker, B. (2013). High levels of psychopathic traits alters moral choice but not moral judgment. Frontiers in Human Neuroscience, 7, 1–6. http://doi.org/10.3389/fnhum.2013.00229

Tassy, S., Oullier, O., Mancini, J., & Wicker, B. (2013). Discrepancies between judgment and choice of action in moral dilemmas. Frontiers in Psychology, 4(MAY), 1–8. http://doi.org/10.3389/fpsyg.2013.00250

Team, R. C. (2016). R: A language and environment for statistical computing. Vienna, Austria: R Foundation for Statistical Computing. Retrieved from https://www.r-project.org/

Thombs, B. D., Bernstein, D. P., Lobbestael, J., & Arntz, A. (2009). A validation study of the Dutch Childhood Trauma Questionnaire-Short Form: factor structure, reliability, and known-groups validity. Child Abuse & Neglect, 33(8), 518–23. http://doi.org/10.1016/j.chiabu.2009.03.001

Tottenham, N., Hare, T. a, Millner, a, Gilhooly, T., Zevin, J. D., & Casey, B. J. (2011). Elevated amygdala response to faces following early deprivation. Developmental Science, 14(2), 190–204. http://doi.org/10.1111/j.1467-7687.2010.00971.x

Ullsperger, M., Harsay, H. A., Wessel, J. R., & Ridderinkhof, K. R. (2010). Conscious perception of errors and its relation to the anterior insula. Brain Structure and Function, 1–15. http://doi.org/10.1007/s00429-010-0261-1

van Baardewijk, Y., Andershed, H., Stegge, H., Nilsson, K. W., Scholte, E., & Vermeiren, R. (2010). Development and Tests of Short Versions of the Youth Psychopathic Traits Inventory and the Youth Psychopathic Traits Inventory-Child Version. European Journal of Psychological Assessment, 26(2), 122–128. http://doi.org/10.1027/1015-5759/a000017

Van der Laan, A. M., & Blom, M. (2006). Jeugddelinquentie: risico's en bescherming. Den Haag.

van Dinteren, R., Arns, M., Jongsma, M. L. A., & Kessels, R. P. C. (2014). P300 development across the lifespan: A systematic review and meta-analysis. PLoS ONE, 9(2). http://doi.org/10.1371/journal.pone.0087347

Van Lien, R., Schutte, N. M., Meijer, J. H., & de Geus, E. J. C. (2013). Estimated preejection period (PEP) based on the detection of the R-wave and dZ/dt-min peaks does not adequately reflect the actual PEP across a wide range of laboratory and ambulatory conditions. International Journal of Psychophysiology, 87(1), 60–69. http://doi.org/10.1016/j.ijpsycho.2012.11.001

van Veen, V., & Carter, C. S. (2002). The timing of action-monitoring processes in the anterior cingulate cortex. Journal of Cognitive Neuroscience, 14(4), 593–602. http://doi.org/10.1162/08989290260045837

Vaughn, M. G., Freedenthal, S., Jenson, J. M., & Howard, M. O. (2007). Psychiatric symptoms and substance use among juvenile offenders: A latent profile investigation. Criminal Justice and Behavior. http://doi.org/10.1177/0093854807304624

Von Borries, A. K. L., Brazil, I. A., Bulten, B. H., Buitelaar, J. K., Verkes, R. J., & de Bruijn, E. R. A. (2010). Neural correlates of error-related learning deficits in individuals with psychopathy. Psychological Medicine, 40(9), 1559–68. http://doi.org/10.1017/S0033291709992017

Wadsworth, M. E. J. (1976). Delinquency, pulse rates and early emotional deprivation. British Journal of Criminology, 16(3), 245–256. http://doi.org/10.1093/oxfordjournals.bjc.a046738

Wartna, B., Blom, M., & Tollenaar, N. (2011). The Dutch recidivism monitor. Den Haag. Retrieved from https://www.wodc.nl/binaries/the-dutch-recidivism-monitor-2011-20110803_tcm28-78143.pdf

Werner, E. E. (2004). Journeys From Childhood to Midlife: Risk, Resilience, and Recovery. Pediatrics, 114(2), 492. http://doi.org/10.1542/peds.114.2.492-a

White, I. R., Royston, P., & Wood, A. M. (2011). Multiple imputation using chained equations: Issues and guidance for practice. Statistics in Medicine, 30(4), 377–399. http://doi.org/10.1002/sim.4067

Wilkowski, B. M., & Robinson, M. D. (2007). Keeping One's Cool: Trait Anger, Hostile Thoughts, and the Recruitment of Limited Capacity Control. Personality & Social Psychology Bulletin, 33(9), 1201–1213. http://doi.org/10.1177/0146167207301031

Woo, C. W., Chang, L. J., Lindquist, M. A., & Wager, T. D. (2017). Building better biomarkers: Brain models in translational neuroimaging. Nature Neuroscience, 20(3), 365–377. http://doi.org/10.1038/nn.4478

Yang, Y., & Raine, A. (2009). Prefrontal structural and functional brain imaging findings in antisocial, violent, and psychopathic individuals: a meta-analysis. Psychiatry Research, 174(2), 81–8. http://doi.org/10.1016/j.pscychresns.2009.03.012

Zahn, T. P., & Kruesi, M. J. (1993). Autonomic activity in boys with disruptive behavior disorders. Psychophysiology. http://doi.org/10.1111/j.1469-8986.1993.tb02086.x

Zijlmans, J., Marhe, R., Van Der Ende, J., Verhulst, F. C., Popma, A., Tiemeier, H., & Van Den Heuvel, O. A. (2017). Children with Obsessive-Compulsive Symptomology in the General Population: Different Subtypes? Journal of Developmental and Behavioral Pediatrics, 38(7), 476–482. http://doi.org/10.1097/DBP.0000000000000467

Samenvatting (summary in Dutch)

Het algemene doel van dit proefschrift was het vergroten van het begrip van de neurale correlaten van verschillende antisociale kenmerken bij multi-probleem jongvolwassenen, en het beoordelen of dergelijke neurobiologische maten kunnen worden gebruikt om de voorspelling van criminele recidive te vergroten. In een grote steekproef van jongvolwassen mannen met multi-problematiek (N = 127, leeftijd 18 tot 27; getrokken uit een grotere steekproef van 696 multi-probleem jonge volwassenen) hebben we gegevens verzameld met behulp van functionele magnetische resonantie beeldvorming, elektro-encefalografie, en fysiologische metingen van het autonome zenuwstelsel. Zodoende konden we het neurobiologische functioneren beoordelen aan de hand van verschillende meettechnieken. We onderzochten hoe kille-emotieloze, impulsief-onverantwoordelijke, en grandioos-manipulatieve psychopathische eigenschappen, en reactieve en proactieve agressie binnen deze populatie geassocieerd zijn met drie relevante processen: morele evaluatie, cognitieve controle, en het functioneren van het autonome zenuwstelsel.

Jongvolwassenen met multi-problematiek in vergelijking met gezonde controles

In vergelijking met gezonde jongvolwassen mannen, vonden we dat multi-probleem jongvolwassenen slechter presteren op verschillende maten. Ten eerste waren ze in hun morele evaluatie van situaties (hoofdstuk 3) in staat om onderscheid te maken tussen immorele en niet-morele situaties, maar deden dit minder goed dan de controles. Terwijl zij neutrale situaties hetzelfde beoordelen als controles (i.e. niet immoreel), beoordelen zij immorele situaties als minder immoreel dan controles en beoordelen zij niet-morele situaties als meer immoreel dan controles. Ten tweede was hun prestatie tijdens een cognitieve controletaak (hoofdstuk 4) slechter dan die van de controles: hun nauwkeurigheid op de taak was significant lager. Hun beoordeling van emoties tijdens droevige filmfragmenten (hoofdstuk 5) verschilde daarentegen niet. Ze herkenden dat karakters in filmfragmenten verdrietig waren en, evenals de controles, identificeerden ze een zekere mate van angst en boosheid. De controles toonden echter geen enkele variatie in hun beoordeling van het geluk (elke controledeelnemer beoordeelde helemaal geen geluk), terwijl sommige multi-probleem jongvolwassenen ook een zekere mate van geluk identificeerden. Dit kan duiden op enige onzekerheid in de multi-probleemgroep met betrekking tot de herkenning van positieve emoties, maar dit is niet nauwkeurig te beoordelen op basis van de huidige gegevens.

Op de neurobiologische maten vonden we slechts weinig verschillen tussen multi-probleem jongvolwassenen en controles. Tijdens de morele evaluatie (hoofdstuk 3) vertoonden de groepen vergelijkbare neurale activiteit in het gehele brein en

dit activeringspatroon van beide groepen was consistent met de hersengebieden die betrokken bleken bij morele evaluatie in eerder onderzoek. Ook het functioneren van het autonome zenuwstelsel in rust en de reactiviteit van het autonome zenuwstelsel op verdriet (hoofdstuk 5) vertoonden geen verschillen tussen de groepen op de beoordeelde maten (i.e. hartslag, respiratoire sinusaritmie, pre-ejectie periode, en huidgeleidingsniveau). We vonden wel verschillen tussen multi-probleem jongvolwassenen en controles op een van de neurale maten van foutverwerking. Multi-probleem jongvolwassenen vertoonden een significant kleinere hersenreactie snel na het maken van een fout, wat duidt op een verminderde automatische foutverwerking. De latere, meer bewuste verwerking van fouten verschilde niet tussen de groepen. Over het algemeen zijn tekorten in het executief functioneren in overeenstemming met de literatuur over antisociaal gedrag (Ogilvie, Stewart, Chan, & Shum, 2011). In het bijzonder kan een verminderde neurale vroegtijdige foutverwerking ten grondslag liggen aan het voortbestaan van problematisch gedrag, omdat fouten als minder betekenisvol kunnen worden ervaren of ervaren (Hajcak et al., 2005).

Een mogelijke verklaring voor het verminderde onderscheid tussen morele en niet-morele gebeurtenissen, het minder goed functioneren van de foutverwerkingstaak, en de verminderde neurale vroegtijdige foutverwerking is het intelligentieniveau van de populatie. Hoewel we het IQ in de controlegroep niet hebben beoordeeld, hebben we deze geselecteerd op een gemiddeld opleidingsniveau, terwijl de multi-probleemgroep een laag gemiddeld IQ van 83 heeft. Daarnaast vonden we dat IQ significant gerelateerd is aan de waardering van niet-morele situaties ($r = -.41$), aan de nauwkeurigheid van de foutverwerkingstaak ($r = .32$), en aan de snelle hersenrespons op fouten ($r = -.19$). In alle gevallen was een hoger IQ gerelateerd aan betere prestaties.

De vergelijking tussen multi-probleem jongvolwassenen met controles wordt echter bemoeilijkt door verschillende factoren. Ten eerste was de omvang van de controlegroep vrij klein (N=27), waardoor de statistische kracht van de groepsanalyses beperkt was. Ten tweede zijn multi-probleem jongvolwassenen een heterogene groep mensen; er bestaat grote variatie in de problemen die zij hebben. Daarom is het moeilijk te beoordelen aan welke kenmerken de verschillen (en overeenkomsten) in gedrag en biologisch functioneren tussen de groepen kunnen worden toegeschreven. Ze kunnen bijvoorbeeld het gevolg zijn van verschillen in externaliserende problemen, verschillen in trauma's in de kindertijd, of verschillen in drugsgebruik. Het is echter ook mogelijk dat subgroepen van multi-probleem jongvolwassenen lijden aan verschillende combinaties van problemen en dat ze gemiddeld genomen vergelijkbaar zijn met controles, maar dat er verschillende clusters van multi-probleem jongvolwassenen aanwezig zijn met een afwijkend functioneren. Het is belangrijk te beseffen dat dit alleen kan worden bestudeerd als het onderzoek naar multi-probleem jongvolwassenen wordt ingebed in groot bevolkingsonderzoek. Dit

komt doordat er geen controlegroep bestaat die varieert op slechts één of enkele parameters, gezien de problematiek waarin we geïnteresseerd zijn meervoudig en onderling gerelateerd is. In hoofdstuk 2 lieten we door middel van clusteranalyse zien dat het gedrag van multi-probleem jongvolwassenen inderdaad clustert binnen profielen die verschillen naar gelang de ernst en de aard van de problemen, maar helaas waren er van te weinig deelnemers (127 van de 696 deelnemers) neurobiologische gegevens beschikbaar om te kunnen beoordelen of deze clusters ook verschilden in neurobiologisch functioneren. Dergelijk onderzoek op grotere schaal kan licht werpen op de diversiteit aan bevindingen in verschillende onderzoekspopulaties.

Neurale correlaten van antisociaal gedrag binnen multi-probleem jongvolwassenen

Dimensionale analyses waarbij drie psychopathische kenmerken (hoofdstuk 3 en 4) of drie psychopathische kenmerken en twee typen agressie (hoofdstuk 5) werden onderzocht, brachten beperkte associaties aan het licht tussen antisociaal gedrag en neurobiologisch functioneren. We vonden verbanden tussen psychopathie en hersenactiviteit tijdens de morele evaluatie in verschillende hersengebieden (hoofdstuk 3). Hier waren specifiek de kille-emotieloze trekken gerelateerd aan verhoogde hersenactiviteit in drie hersengebieden: de linker ventromediale prefrontale cortex, de linker superieure temporele gyrus, en de linker cingulate gyrus. Voor beide maten van neurale foutverwerking (hoofdstuk 4) en voor de rustactiviteit en reactiviteit van het autonome zenuwstelsel (hoofdstuk 5) vonden we geen relaties tussen antisociale gedragingen en neurobiologische maten.

Onze bevindingen over de morele evaluatietaak suggereren dat de kille-emotieloze trekken van psychopathie gerelateerd kunnen zijn aan wijdverbreide veranderde activeringspatronen tijdens morele evaluatie, in plaats van meer exclusief aan de ventromediale prefrontale cortex en amygdala zoals gesuggereerd door theoretische modellen (Blair, 2007). Andere studies hebben negatieve relaties gevonden tussen amygdala-activiteit en psychopathie in morele paradigma's, maar alleen in tegenstelling tot neutrale stimuli (i.e. immoreel + niet-morele > neutrale, immorele > neutrale, en niet-morele > neutrale contrasten) (Harenski, Edwards, et al., 2014a; Harenski, Harenski, et al., 2014; Harenski et al., 2010). Een beperking van de analyse van deze contrasten is dat het zowel de valentie als de morele waarde van stimuli omvat, in plaats van alleen de morele waarde. Dit bemoeilijkt de interpretatie van de associatie tussen psychopathie en hersenactiviteit, omdat de associatie het gevolg kan zijn van de valentie, de morele waarde, of beide. Het kan zijn dat amygdala disfunctie relevant is voor de morele verwerking, juist omdat het betrokken is bij een affectieve verwerkingscomponent die nodig is om morele

beoordelingen te maken. Bijvoorbeeld als de morele evaluatie (deels) gedreven zou worden door het gevoel dat er iets mis is. Een andere mogelijkheid is dat de morele beoordeling geen affectieve verwerking vereist, maar de twee zijn gecorreleerd omdat immorele handelingen voor de meeste mensen een negatieve valentie hebben. Ten slotte zou binnen psychopathie het affectieve proces minder relevant kunnen zijn voor de morele beoordeling. Welke verklaring het beste past, vereist meer specifiek onderzoek, maar de resultaten van één onderzoek bij gezonde vrijwilligers suggereren wel dat de betrokkenheid van de amygdala varieert met hoe emotioneel de geëvalueerde morele situaties zijn en dat binnen psychopathie de betrokkenheid van de amygdala minder groot is (Glenn et al., 2009a).

Met betrekking tot foutverwerking voegen onze resultaten toe aan het bestaande bewijs dat neurale vroege foutverwerking intact is binnen psychopathie (e.g. Brazil et al., 2009; Maurer et al., 2015, 2018), maar de nul-bevindingen over alle drie de psychopathische factoren voor neurale late foutverwerking zijn moeilijker te interpreteren. Een verklaring zou kunnen zijn dat initiële foutverwerkingstekorten in de adolescentie veranderen in foutverwerkingsovercompensatie op volwassen leeftijd (waar een positieve associatie tussen late foutverwerking en psychopathie is gemeld (Steele, Maurer, et al., 2015). Een andere mogelijkheid is dat de nul-bevinding te wijten is aan het gebruik van een zelfrapportage vragenlijst van psychopathie.

Ook onze nul-bevindingen voor de autonome maten van het zenuwstelsel in relatie tot alle antisociale maten zijn enigszins raadselachtig, aangezien een afwijkende autonome activiteit in rust een robuuste bevinding is in studies naar antisociaal gedrag (e.g. Lorber, 2004; Ortiz & Raine, 2004; Portnoy & Farrington, 2015). Dit kan deels worden verklaard door het feit dat de effectgroottes bij volwassenen ongeveer twee keer zo klein zijn als bij kinderen (Portnoy & Farrington, 2015) en dus moeilijker te detecteren zijn. Natuurlijk is het ook mogelijk dat er binnen multi-probleem jongvolwassenen geen relatie bestaat tussen antisociaal gedrag en het functioneren van het autonome zenuwstelsel. Dit kan het geval zijn als afwijkend autonoom functioneren specifiek aanwezig zou zijn in bepaalde subgroepen met extreme niveaus van asociaal gedrag. Echter hebben we in hoofdstuk 5 wel laten zien dat rusthartslag longitudinaal voorspellend is voor criminele recidive binnen multi-probleem jongvolwassenen, wat aangeeft dat het binnen onze steekproef gerelateerd is aan crimineel gedrag, ongeacht het feit dat het niet gerelateerd is aan psychopathie of agressie.

Er zijn verschillende beperkingen te overwegen met betrekking tot onze dimensionale bevindingen. Ten eerste, omdat multi-probleem jongvolwassenen een zeer antisociale steekproef vormen, bestaat het risico dat er binnen de groep te weinig variatie is op de psychopathie- en agressiematen of dat relatief veel van de variatie bestaat uit meetfouten in plaats van echte variatie. Aangezien de individuele scores op de maten echter het hele spectrum bestrijken, lijkt dit niet waarschijnlijk.

Ten tweede maakt de manier waarop de psychopathie werd gemeten het moeilijk om te vergelijken met ander onderzoek. Waar een groot deel van de onderzoeken gebruik maakt van de Psychopathy Checklist - Revised of de Psychopathy Checklist Youth Version (Hare, 2003), die zowel gegevens uit een uitgebreid interview als dossiergegevens bevat, hebben we gebruik gemaakt van de YPI (van Baardewijk e.a., 2010). Hoewel de conceptualisaties van psychopathie van verschillende instrumenten overlappen, zijn er enkele verschillen tussen de maten. Het belangrijkste is of crimineel gedrag wordt gezien als onderdeel van het psychopathisch construct (Hare & Neumann, 2008) of als een gevolg van psychopathie (Cooke & Michie, 2001). In de YPI is crimineel gedrag niet opgenomen in de definitie. Dit kan deels verklaren waarom we geen associaties hebben gevonden tussen de YPI en fysiologische maten (hoofdstuk 3 en 4), maar wel vinden dat deze fysiologische maten voorspellend zijn voor toekomstige delinquentie (hoofdstuk 5).

Neurovoorspelling van delinquentie

In hoofdstuk 5 hebben we de incrementele voorspellende waarde van neurobiologische maatregelen onderzocht naast de bekende risicofactoren voor algemene en ernstige criminele recidive binnen multi-probleem jongvolwassenen. Uit de bekende risicofactoren vonden we delict geschiedenis, proactieve en reactieve agressie en de impulsief-onverantwoordelijke psychopathische factor als goede individuele voorspellers. Uit de neurobiologische metingen vonden we dat hartslag in rust en twee hersenresponsen op het maken van fouten goede individuele voorspellers zijn. Deze groep van drie neurobiologische variabelen vergrootte de voorspellende kracht van de modellen. Met name in de analyse van ernstige recidive verbeterden deze maten de voorspellende functie.

Onze bevindingen komen overeen met eerder onderzoek waaruit blijkt dat rusthartslag een sterke voorspeller is van gewelddadige delinquentie (Latvala et al., 2015). De enige andere studie die de voorspellende waarde van EEG-metingen van foutverwerking beoordeelde vond geen effecten om delinquentie bij volwassen daders te voorspellen. Naar aanleiding van een eerder onderzoek, waarbij werd aangetoond dat activiteit in de anterieure cingulate cortex tijdens een inhibitie taak voorspellend was voor recidive (Aharoni et al., 2013), hebben we activiteit uit hetzelfde gebied gemeten tijdens een vergelijkbare taak. De voorspellende bevinding konden we echter niet repliceren.

Wetenschappelijke implicaties en toekomstig onderzoek

Om ons begrip van neurobiologische processen in antisociale populaties te bevorderen, moeten deze processen worden onderzocht vanuit een meer ontwikkelingsgericht perspectief. Grote en langdurige cohortstudies zijn nodig om de ontwikkeling van de relaties tussen antisociaal gedrag en neurobiologie te beoordelen, aangezien deze in de loop van de tijd kunnen veranderen en variëren tussen verschillende ontwikkelingsfasen (zie hoofdstuk 4 en 5). Rekening houdend met de natuurlijke ontwikkeling van deze processen kan licht werpen op de vraag waarom de bevindingen verschillen tussen populaties van verschillende leeftijden. Daarnaast is het relevant om naturalistische groepen te onderzoeken, zoals multi-probleem jongvolwassenen, omdat bevindingen in klinische steekproeven kunnen verschillen van die binnen ongeselecteerde steekproeven.

De bevindingen van onze longitudinale studie (hoofdstuk 6) suggereren dat het toevoegen van neurobiologische maatregelen aan risicobeoordelingen een manier kan zijn om de voorspelling van recidive te verbeteren. Tot nu toe zijn er te weinig studies uitgevoerd om de implementatie van dit type risicobeoordeling in de praktijk te rechtvaardigen, maar het empirische bewijs voor een dergelijke risicobeoordeling neemt toe. Aangezien de voorspelling waarschijnlijk deels een ander deel van de te verklaren variantie omvat dan bekende risicofactoren zoals de geschiedenis van criminaliteit en het drugsgebruik, kunnen neurobiologische maatregelen de kwaliteit van de risicobeoordeling in de rechtspraktijk in theorie aanzienlijk verbeteren. Een dergelijke neurobiologisch geïnformeerde beoordeling kan nuttig zijn in besluitvormingsprocessen, bijvoorbeeld met betrekking tot behandeling en proeftijd. Wanneer we de relatie tussen neurobiologie en antisociaal gedrag proberen te begrijpen is het essentieel dat we ons mechanistisch inzicht verbeteren, echter als we neurobiologische maatregelen inzetten als hulpmiddelen om antisociaal gedrag te voorspellen, is het in eerste instantie niet nodig om te begrijpen hoe en waarom dit het geval is (Moons, Royston, Vergouwe, Grobbee, & Altman, 2009). Aangezien ons mechanistisch begrip van deze processen nog zeer beperkt is, verwacht ik dat dit soort voorspellende modellering op korte termijn een van de meest rationele en effectieve manieren zal zijn om neurobiologische bevindingen in de klinische en gerechtelijke praktijk te implementeren.

Naast de vraag of voorspellingsmodellen met neurobiologische maatregelen voldoende betrouwbaar kunnen zijn, is het relevant om te beoordelen hoe haalbaar het is om dergelijke gegevens buiten de laboratoriumomgeving en zonder al te hoge kosten te verkrijgen. Zelfs als bijvoorbeeld een fMRI-maat de voorspellende kracht van een model voor delinquentie robuust zou vergroten, beperken de hoge kosten en de complexe apparatuur de bruikbaarheid ervan in veel situaties. Daarentegen zijn fundamentele fysiologische maten vrij eenvoudig te verwerven, is er weinig

expertise voor nodig, en zijn ze zeer goedkoop. Elektro-encefalografische maten liggen hiertussen in en vereisen meer gegevensverwerking voordat ze bruikbare variabelen opleveren. In toekomstige studies is replicatie van de fysiologische en hersenbevindingen nodig. Deze studies moeten worden uitgevoerd in grotere en kruislings gevalideerde steekproeven om de robuustheid van het voorspellingsmodel te beoordelen, en moeten plaatsvinden in instellingen waar de feitelijke implementatie zou kunnen plaatsvinden, zoals gevangenissen.

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Curriculum vitae and publications

Curriculum vitae

Josjan Zijlmans was born on April 13th 1989 in Rotterdam, The Netherlands. After completing secondary education, he studied psychology at the Erasmus University Rotterdam, where he graduated cum laude in 2012. Subsequently he worked as an academic teacher at the Institute of Psychology at the Erasmus University Rotterdam. In 2013 he started his PhD at the Department of Child and Adolescent Psychiatry of the VUmc, focusing on the neurobiology underlying antisocial behavior within multi-problem young adults. The results of that research are described in this dissertation. He is currently working as a post-doctoral researcher in the same department where he carried out his doctoral research. In this position he is engaged in setting up a large-scale, multi-center cohort within Dutch child and adolescent psychiatry. In addition, he coordinates an interdisciplinary course on the neurobiology, history, and therapeutic application of psychedelics as part of the Honours Program of the Vrije Universiteit in Amsterdam.

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Josjan Zijlmans is geboren op 13 april 1989 te Rotterdam. Na zijn gymnasiumexamen studeerde hij psychologie aan de Erasmus Universiteit Rotterdam, waar hij in 2012 *cum laude* afstudeerde. Vervolgens werkte hij als wetenschapelijk docent bij het Instituut voor Psychologie aan de Erasmus Universiteit Rotterdam. In 2013 startte hij zijn promotie-onderzoek aan de afdeling Kinder- en Jeugdpsychiatrie van het VUmc, gericht op de neurobiologie onderliggend aan antisociaal gedrag binnen multi-probleem jongvolwassenen. De resultaten van dat onderzoek zijn in dit proefschrift beschreven. Momenteel is hij werkzaam als post-doctoraal onderzoeker bij dezelfde afdeling waar hij zijn promotieonderzoek verrichtte. In deze functie houdt hij zich bezig met het opzetten van een grootschalig, multi-center cohort binnen de Nederlandse kinder- en jeugdpsychiatrie. Daarnaast coördineert hij in het kader van het Honours Program van de Vrije Universiteit een interdisciplinaire cursus over de neurobiologie, geschiedenis, en therapeutische mogelijkheden van psychedelica.

Publications

Published

Zijlmans, J., Van Duin, L., Jorink, M., Marhe, R., Luijks, M.J.A., Crone, M.R., Popma, A., Bevaart, F. (2020). Disentangling multi-problem behavior in young adults: a cluster analysis. *Development and Psychopathology*

Zijlmans, J., Bevaart, F., Van Duin, L., Luijks, M.J.A., Popma, A., Marhe, R. (2019) Error-related brain activity in relation to psychopathic traits in multi-problem young adults: an ERP study. *Biological Psychology*

Zijlmans, J., Marhe, R., Bevaart, F., Luijks, M.J.A., Van Duin, L., Tiemeier, H., Popma, A. (2018) Neural correlates of moral evaluation and psychopathic traits in male multi-problem young adults. *Frontiers in Psychiatry*

Zijlmans, J., Marhe, R., Van der Ende, J., Verhulst, F., Popma, A., Tiemeier, H., van den Heuvel, O. (2017) Children with Obsessive-Compulsive Symptoms in the General Population: Different Subtypes? *Journal of Developmental & Behavioral Pediatrics*

Van Dongen, N.N.N. & **Zijlmans, J.** (2017) The Science of Art: The Universality of the Law of Contrast. *American Journal of Psychology* [shared first author]

Van Duin., L., Bevaart, F., **Zijlmans, J.**, Luijks, M.J.A., Doreleijers, T.A.H., Wierdsman, A.I., Oldehinkel, A.J., Marhe, R., Popma, A. (2018) The role of adverse childhood experiences and mental health care use in psychological dysfunction of male multi-problem young adults. *European Child & Adolescent Psychiatry*

Luijks, M., Bevaart, F., **Zijlmans, J.**, van Duin, L., Marhe, R., Doreleijers, T.A.H., Tiemeier, H., Asscher, J., Popma, A. (2017) A multimodal day treatment program for multi-problem young adults: Study protocol for a randomized controlled trial. *Trials*

Van Duin, L. & Bevaart, F., Paalman, C.H., Luijks, M.J.A., **Zijlmans, J.**, Marhe, R., Blokland, A.J., Doreleijers, T.A.H., Popma, A. (2017). Child Protection Service interference in childhood and the relation with mental health problems and delinquency in young adulthood: a latent class analysis study. *Child and Adolescent Psychiatry & Mental Health*

Tielbeek, J., Al-Itejawi, Z., **Zijlmans, J.**, Polderman, T., Buckholtz, J., Popma, A. (2016) The impact of chronic stress during adolescence on the development of aggressive behavior. *Neuroscience & Biobehavioral Reviews*

Dijkstra, K., Eerland, A., **Zijlmans, J.**, Post, L. (2014) Embodied cognition, abstract concepts, and the benefits of new technology for implicit body manipulation. *Frontiers in Psychology*

Dijkstra, K., Eerland, A., **Zijlmans, J.**, Post, L. (2012) How body balance influences political party evaluations: a Wii balance board study. *Frontiers in Psychology*

In revision / In submission

Zijlmans J., Marhe, R., Bevaart, F., Van Duin, L., Luijks, M.J.A., Franken, I.H.A., Tiemeier, H., Popma, A. The predictive value of neurobiological measures for recidivism in delinquent young adults.

Zijlmans, J., Marhe, R., Luijks, M.J.A., Van Duin, L., Bevaart, F., Popma, A. No association between antisocial behavior and autonomic functioning in multi-problem young adults.

van Duin, L., van Delft, I., Bevaart, F., **Zijlmans, J.**, Luijks, M.J.A., Doreleijers, Th.A.H., Marhe, R., Popma, A. Can social relationship qualities explain the association between child maltreatment and quality of life in male multi-problem young adults?

van Duin, L., de Vries Robbé, M., Marhe, R., Bevaart, F., **Zijlmans, J.**, Luijks, M.J.A., Doreleijers, Th.A.H., Popma, A. Criminal careers and adverse childhood experiences related to recidivism and successful community functioning.